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☐	L2	L1 and (nf or nfkappa or nf-kappab or nf-kappa-b)	4
☐	L3	(nf or nfkappa or nf-kappab or nf-kappa-b).ti,ab,clm.	5299
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☐	L12	cgpc	26
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L8: Entry 1 of 30 File: PGPB Aug 19, 2004

DOCUMENT-IDENTIFIER: US 20040162309 A1
TITLE: Methods and compositions related to IRM compounds and toll-like receptor 8

Detail Description Paragraph:
[0101] (b) bacterial diseases such as, for example, diseases resulting from infection by bacteria of, for example, the genus Escherichia, Enterobacter, Salmonella, Staphylococcus, Shigella, Listeria, Aerobacter, Helicobacter, Klebsiella, Proteus, Pseudomonas, Streptococcus, Chlamydia, Mycoplasma, Pneumococcus, Neisseria, Clostridium, Bacillus, Corynebacterium, Mycobacterium, Campylobacter, Vibrio, Serratia, Providencia, Chromobacterium, Brucella, Yersinia, Haemophilus, or Bordetella;

CLAIMS:

11. The method of claim 4 wherein administering the IRM compound modulates NF-.kappa.B activity, the production of at least one cytokine, the production of at least one co-stimulatory marker, the production of an intercellular adhesion molecules, the production of a maturation marker, or any combination thereof.

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L8: Entry 3 of 30 File: PGPB Jul 29, 2004

DOCUMENT-IDENTIFIER: US 20040146526 A1
TITLE: Inhibition of NF-kappaB activation

Abstract Paragraph:
A H. pylori thioredoxin protein having a seq ID No. 1 is capable of inhibiting the activation of NF-.kappa.B. The protein may be used in treating inflammation.

Summary of Invention Paragraph:
[0006] According to the invention there is provided a H. pylori protein or derivative or fragment or mutant or variant thereof capable of inhibiting the activation of NF-.kappa.K.

Summary of Invention Paragraph:
[0007] Preferably the protein is a thioredoxin or derivative or fragment or mutant or variant thereof.

Summary of Invention Paragraph:
[0009] The invention also provides a thioredoxin or derivative or fragment or mutant mutant or variant thereof containing the redox active peptide sequence CGPC capable of inhibiting the activation of NF-.kappa.B.

Summary of Invention Paragraph:
[0010] The invention further provides prokaryotic or eukaryotic thioredoxins having potent immune-suppressive effects.

Summary of Invention Paragraph:
[0011] The invention also provides polypeptides containing the redox active peptide sequence CGPC, capable of inhibiting the activation of NF-.kappa.B.

Summary of Invention Paragraph:
[0012] The invention also provides a H. pylori protein having the following amino acid sequence:

Summary of Invention Paragraph:
[0013] The invention further provides use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof of the invention in a method for the prevention and/or treatment of inflammation, such as for the prevention and/or treatment of inflammatory bowel disease.

Summary of Invention Paragraph:
[0014] The invention also provides use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof of the invention in a method for the prevention and/or treatment of rheumatoid/autoimmune arthritis, or other autoimmune diseases, asthma, septic shock, lung fibrosis, glomerulonephritis, atherosclerosis, autoimmune encephalomyelitis or any chronic disease wherein NF-.kappa.B is transcriptionally activated.

Summary of Invention Paragraph:
[0015] The invention also provides use of a H. pylori thioredoxin protein or

derivative or fragment or mutant thereof of the invention in blood transfusions and soft tissue injury.

Summary of Invention Paragraph:
[0016] The invention also provides a H. pylori thioredoxin protein or derivative or fragment or mutant thereof of the invention for use in the preparation of a medicament in the treatment and/or prophylaxis of any chronic disease wherein NF-.kappa.B is transcriptionally activated.

Brief Description of Drawings Paragraph:
[0019] FIG. 1 is an autoradiograph showing the results of an electrophoretic mobility shift assay (EMSA) showing the effect of H. pylori thioredoxin on constitutive NF-.kappa.B activity in AGS cells (an adenocarcinoma cell line);

Brief Description of Drawings Paragraph:
[0020] FIG. 2 is an autoradiograph showing the results of an EMSA showing the time course of NF-.kappa.B inhibition upon treatment of AGS cells with H. pylori thioredoxin;

Brief Description of Drawings Paragraph:
[0021] FIG. 3 is an autoradiograph showing the results of an EMSA showing the effects of H. pylori thioredoxin on H. pylori-induced NF-.kappa.B activation in AGS cells;

Brief Description of Drawings Paragraph:
[0022] FIG. 4 is an autoradiograph showing the results of an EMSA showing the effect of H. pylori thioredoxin on NF-.kappa.B activation by various stimuli;

Brief Description of Drawings Paragraph:
[0023] FIG. 5 is an autoradiograph showing the results of an EMSA showing the inhibition of H. pylori-induced NF-.kappa.B by H. pylori thioredoxin post stimulation with H. pylori; and

Brief Description of Drawings Paragraph:
[0024] FIG. 6 is a SDS-PAGE gel showing the identification of AGS cell proteins reduced specifically by H. pylori thioredoxin.

Brief Description of Drawings Paragraph:
[0025] FIG. 7 is a FACscan analysis demonstrating the down-regulatory effect of thioredoxin on the surface expression of CD44 and ICAM-1 on AGS cells treated with or without H. pylori.

Detail Description Paragraph:
[0027] We have found a method for the prevention and reversal of NF-.kappa.B activation in mammalian cells by addition of effective inhibiting amounts of a H. pylori thioredoxin either alone or in combination with a thioredoxin reductase regenerating system. The H. pylori thioredoxin may be in the form of the whole recombinant protein or a fragment or derivative or mutant or variant thereof.

Detail Description Paragraph:
[0028] We have found that recombinant thioredoxin from the gastric pathogen H. pylori is a potent inhibitor of NF-.kappa.B activation in vitro. When added exogenously to AGS cells (an adenocarcinoma cell line) in vitro, low doses of H. pylori thioredoxin (1-20 .mu.g/ml; 70 nM to 1.4 .mu.M) inhibit constitutive NF-.kappa.B activity. In addition, H. pylori thioredoxin completely abrogates the pronounced NF-.kappa.B activity observed in AGS cells when NF-.kappa.B DNA binding activity is activated by a variety of external stimuli including proinflammatory cytokines and phorbol esters. H. pylori Trx was found to prevent NF-.kappa.B activation both prior to stimulation (FIGS. 1 to 4) with inducers of NF-.kappa.B and secondary to induction of NF-.kappa.B (FIG. 5). Preliminary experiments (FIG.

6) indicate that H. pylori Trx interacts specifically with target proteins in AGS cells as demonstrated by the incorporation of the thiol-specific fluorescent probe, monobromobimane, into Trx-treated AGS cells. The precise mechanism of Trx-modulated NF-.kappa.B activity has yet to be fully elucidated. H. pylori thioredoxin also down-regulates the resting and inducible surface expression of CD44 and the adhesion molecule ICAM-1 (FIG. 7)

Detail Description Paragraph:
[0029] The ability of H. pylori thioredoxin to inhibit NF-.kappa.B activation in vitro suggest a potential therapeutic utility for thioredoxin as a novel approach for the treatment of patients with chronic inflammatory disease states such as autoimmunic arthritis, asthma, septic shock, lung fibrosis, glomerulonephritis, atherosclerosis, autoimmune encephalomyelitis, cystic fibrosis, rheumatoid arthritis, systemic inflammatory response syndrome and other NF-.kappa.B-mediated inflammatory disease states.

Detail Description Paragraph:
[0030] The present invention provides a protein, H. pylori thioredoxin, comprising a redox-active motif (CGPC), (cysteine-glycine-proline-cyseine-), capable of inhibiting activation of the transcription factor NF-.kappa.B.

Detail Description Paragraph:
[0033] The present invention also includes within its scope peptides derived from H. pylori thioredoxin identified above where such derivatives have redox-activity or or where such derivatives inhibit NF-.kappa.B activation. These derivatives will normally be peptide fragments of the native protein which include the redox-active motif, but can also be functionally equivalent variants of the recombinant thioredoxin modified by well known techniques such as site-directed mutagenesis. For For example, it is possible by such techniques to substitute amino acids in a sequence with equivalent amino acids. Groups of amino acids known to be normally equivalent are:

Detail Description Paragraph:
[0034] Thioredoxin variants can be obtained by conventional gene engineering technology. For example, the amino acid sequence and base sequence of thioredoxin are known and described in numerous documents in the scientific literature. Based on the prior art documents, cDNA encoding natural thioredoxin can be obtained from an appropriate cDNA library. A variant can then be obtained by, for example, site-directed mutagenesis (9).

Detail Description Paragraph:
[0037] The thioredoxin of the invention may be produced by isolation from H. pylori, using conventional purification techniques. However, it is recognised that for production of the protein in commercial quantities, production by synthetic routes is desirable. Such routes include the stepwise solid phase approach and production using recombinant DNA techniques. The latter route is preferred.

Detail Description Paragraph:
[0038] Stated generally, the production of thioredoxin by recombinant DNA techniques involves the transformation of a suitable host organism or cell with an expression vector including a DNA sequence coding for thioredoxin, followed by the culturing of the transformed host and subsequent recovery of the expressed thioredoxin. Such techniques are described generally in Sambrook et al. Molecular Cloning, 2nd edition, Cold Spring Harbour Press (1987).

Detail Description Paragraph:
[0039] The redox protein thioredoxin and the associated enzyme thioredoxin reductase reductase (TR) constitute a thiol-dependent reduction-oxidation system that can catalyse the reduction of certain proteins by NADPH (10).

Detail Description Paragraph:
[0040] In its primary aspect, the present invention is directed to the provision of thioredoxin which is protective against inflammation. Subjects which are susceptible susceptible to inflammation are mammals including humans.

Detail Description Paragraph:
[0041] The concentration of thioredoxin which can be used ranges from about 1 .mu.M to about 30 .mu.M. The optimal concentration for intact reduced H. pylori thioredoxin appears to be a least 10 .mu.M.

Detail Description Paragraph:
[0042] The thioredoxin compound may be orally administered to a patient requiring such treatment on a regular basis over an extended period of time. Alternatively, the compound may be administered directly to the localised site of inflammation.

Detail Description Paragraph:
[0043] It should be recognised that the precise level of thioredoxin can be readily ascertained by a person skilled in the art in light of the present invention.

Detail Description Paragraph:
[0044] Thioredoxin and thioredoxin derived derivatives, fragments or mutants thereof thereof may be administered directly, in the form of a formulation or any other pharmaceutically acceptable manner. Preferably such formulation includes an ingestable carrier which is a pharmaceutically acceptable carrier such as a capsule, tablet or powder. The formulation may also include a drug entity.

Detail Description Paragraph:
[0046] Materials and Methods Used in the Purification of Thioredoxin from H. pylori and Inhibition of NF-.kappa.B Activity.

Detail Description Paragraph:
[0047] Materials 2',5'-ADP-agarose, Cibacron Blue 3GA, iminodiacetic acid-Sepharose 6B, .rho.-aminobenzamidine-agarose, DTT (1,4-dithio-DL-threitol), E. coli thioredoxin and anti-E. coli thioredoxin were obtained from Sigma Chemical Co. Ltd., Ltd., Poole, Dorset, U.K. Sephacryl S-300 was obtained from Pharmacia Biotech, Uppsala, Sweden. Isopropyl-.beta.-D-thiogalactoside, NADPH, NADP+, and NADH were obtained from Boehringer Mannheim, Bell Lane, Lewes, East Sussex, UK. DEAE-52 was purchased from Whatman (Maidstone, UK). Factor Xa was purchased from New England Biolabs, Hertfordshire, U.K. All buffer reagents for SDS-PAGE were prepared in deionised water. The human gastric cancer cell line AGS and HuT 78, sezary lymphoma cells, were obtained from the European collection of Animal Cell Cultures (ECACC, Porton Down, Salisbury, UK). RPMI 1640 medium, fetal calf serum, penicillin, streptomycin, L-glutamine, Hank's Balanced salt solution (HBSS) and trypsin were obtained from GIBCO BRL, life technologies Renfrewshire, Pasiley, Scotland. NF-.kappa.B consensus oligonucleotide was from Promega, poly(dI-dC) was from Pharmacia, Biosystems, Milton Keynes, UK. [.gamma..sup.32P]ATP (35 pmol, 3000 Ci/mmol) was from Amersham International (Aylesbury, UK). Bovine albumin, ammonium persulphate, Nonidet P-40, PMA, IL-1 and PMSF were obtained from Sigma (Poole, Dorset, UK and St. Louis, Mo., USA). All other chemicals were of analytical reagent grade.

Detail Description Paragraph:
[0050] Bacterial strain and growth conditions. The reference strains of H. pylori used in this study (NCTC 11638 and 11637) were obtained from the National Collection of Type Cultures, Public Health Laboratory, London, U.K. All components for H. pylori culture media were obtained from Oxoid, Unipath Ltd., Basingstoke, Hampshire, U.K. H. pylori was grown under microaerobic conditions (Oxoid Campylobacter system, 5% O.sub.2, 10% CO.sub.2) for 4 days on 7% lysed horse blood Columbia agar at 37.degree. C. Bacteria were harvested into RPMI medium without antibiotics and resuspended to yield a concentration of 6.times.10.sup.8

organisms/ml and used immediately.

Detail Description Paragraph:
[0051] Purification of thioredoxin reductase (TR). Agar-grown H. pylori was suspended in buffer A (20 mM Tris-HCl, pH 7.5) and subjected to sonication (4.times.1 min bursts) on ice using a Branson sonifier 450. After centrifugation to remove intact cells and cellular debris (12, 000.times.g, 10 min, 4.degree. C.) the resulting supernatant was applied to a DEAE cellulose column (3.5.times.16 cm) equilibrated in buffer A. Thioredoxin reductase activity was eluted with a gradient (300 ml) of KCl (0-0.35 M) in buffer A. Active fractions were pooled, dialyzed against buffer B (50 mM Tris-HCl, pH 7.5) and applied to a Cibacron Blue 3GA column (1.times.3 cm). TR was eluted with a gradient of KCl (0-0.4 M). Active fractions were pooled, dialyzed against buffer B and applied to a small 2',5'-ADP agarose column (1 ml). Thioredoxin reductase was eluted upon application of 0.2 M KCl. The ion exchange and dye affinity chromatography steps were performed at room temperature and the ADP-Sepharose step was done at 4.degree. C.

Detail Description Paragraph:
[0052] Gel filtration chromatography. A sonicate of H. pylori was prepared as described above and 0.5 ml (.about.10 mg protein/ml) of the material was applied to a column (diameter 1.5 cm; height 29.7 cm) of Sephacryl S-300 superfine (Pharmacia) equilibrated with phosphate buffered saline (pH 7.5) containing NaN.sub.3 (0.02%, w/v). The protein was eluted with this same buffer (8.5 cm/h) and the collected fractions were assayed for both TR activity and total protein. The column was first calibrated with proteins of known molecular size (Pharmacia). Gel filtration over Sephadex G-50 (Pharmacia) was performed also in phosphate buffered saline (PBS).

Detail Description Paragraph:
[0053] Measurement of thioredoxin reductase activity. Thioredoxin reductase activity activity was assayed at 25.degree. C. in 0.1 M potassium phosphate buffer (pH 7.5) containing EDTA (1 mM), DTNB (5 mM) and NADPH (0.2 mM) in a final volume of 1.0 ml. The reaction was initiated by the addition of enzyme and the progress of the reaction was monitored by the increase in absorbance at 412 nm in a Pye Unicam 5625 spectrophotometer. One unit of enzyme activity is defined as the amount of enzyme required to oxidize one .mu.mol of NADPH per minute at 25.degree. C., pH 7.5. Activity was calculated as .mu.mol NADPH oxidized/min in accordance with the relationship .DELTA.A412/(13.6.times.2). Thioredoxin reductase activity was assayed also using a minor modification of the insulin reduction assay (12). The reaction mixture consisted of 0.1 M potassium phosphate buffer (pH 7.0) containing EDTA (1 mM), insulin (0.1 mg/ml), NADPH (0.2 mM) and H. pylori histidine-tagged Trx (2 .mu.M) in a final volume of 1 ml. The reaction was initiated by the addition of the enzyme to the mixture at 25.degree. C. and the oxidation of NADPH was monitored at 340 nm. The amount of NADPH oxidized was determined from the relationship .DELTA.A340/6.2.

Detail Description Paragraph:
[0054] Purification of native H. pylori Trx. Thioredoxin (Trx) was purified by a combination of ion exchange chromatography on DEAE cellulose and gel filtration over Sephadex G-50. Fractions containing Trx were identified using the spectrophotometric insulin reduction assay (12).

Detail Description Paragraph:
[0055] Expression and purification of recombinant H. pylori Trx. Transformants of E. coli BL21(DE3)pLysS with plasmid pET-16b (Novagen) containing the Trx gene (HP 824) were grown at 37.degree. C. in LB broth supplemented with ampicillin (100 .mu.g/ml) and chloramphenicol (30 .mu.g/ml). H. pylori Trx was expressed as an N-terminal decahistidine fusion protein in E. coli. The gene coding for Trx was amplified by PCR using Expand.TM. (Boehringer Mannheim), using the amplification conditions recommended by the manufacturer. Under these conditions a single product was obtained and this was cloned into the expression plasmid via the BamHI and NdeI

restriction sites. The following primers were used: forward primer, 5'-CGCCATATGAGTCACTATATTGAATTAAC-3'; reverse primer 5'-CGCGGATCCGCCTAAGAGTTTGTTCAATTG-3'. Overexpression of the fusion protein was induced by adding 1 mM isopropyl-.beta.-D-thiogalactoside at exponential phase and the incubation continued for 3 h at 37.degree. C. The induced cells were harvested by centrifugation (10,000.times.g, (10,000.times.g, 15 min, 4.degree. C.), washed once with 50 mM Tris HCl (pH 7.5) and and subjected to sonication (3.times.1 min). The soluble fusion protein was purified purified to homogeneity by metal chelate chromatography on a Ni.sup.2+ column (3 ml) ml) according to the manufacturer's instructions. The protein was eluted with 0.4 M imidazole in 20 mM Tris HCl (pH 7.5) containing 0.5 M NaCl. Typically, 2-3 mg of homogenous Trx/100 ml culture was obtained by this procedure. Both the histidine tagged fusion protein and the recombinant Trx obtained after cleavage of the histidine tail by Factor Xa were indistinguishable in their spectroscopic properties properties and redox behaviour.

Detail Description Paragraph:
[0056] Sequence analysis Multiple sequence alignments were made with the Clustal program. Amino-terminal sequence analysis of purified H. pylori Trx and TR was performed by Ms. Aine Healy at the National Food Biotechnology Centre, University College Cork using an Applied Biosystems automated sequencer.

Detail Description Paragraph:
[0058] Coculture of AGS cells with H. pylori and other stimuli Confluent AGS cells were cocultured with or without H. pylori (6.times.10.sup.8 cfu/ml) or exposed to the cytokines interleukin-1beta (IL-1 .beta.) (10 ng/ml) and tumor necrosis factor-alpha (TNF-.alpha.) (20 ng/ml) or the mitogen phorbol 13-myristate 12-acetate (PMA) (20 ng/ml).

Detail Description Paragraph:
[0061] Cell proliferation and toxicity assays AGS cells (1.times.10.sup.5 cells/ml) were cultured in 96-well plates in triplicate overnight at 37.degree. C. The cells were then incubated with or without thioredoxin for various periods of time, as indicated where appropriate, at 37.degree. C. To the cultured cells, 20 .mu.l of freshly prepared PMS/MTS solution was added to each well and the plates were incubated for 4 h at 37.degree. C. The absorbance of these wells was read at 490 nm using an ELISA plate reader. The average of the triplicate readings was taken for each sample. Under the experimental conditions and in the range of thioredoxin concentrations used, the cell viability was greater than 90%.

Detail Description Paragraph:
[0062] Flow cytometry analysis AGS cells were grown to confluence on 6-well plates and then incubated with or without thioredoxin (10 .mu.g/ml) for 2 h at 37.degree. C. The cells were then stimulated with H. pylori for 24 h at 37.degree. C. The cells were washed with PBS and incubated for 30 min with antibodies to CD44 (L3D.1) and ICAM-1 at room temperature followed by washing and labelling with fluorescein isothiocynate (FITC)-conjugated rabbit F(ab).sub.2' anti-mouse IgG (Dakopotts, Glostrup, Denmark). Samples were analysed by flow cytometry in a FAC scan (Becton Dickinson, Mountain View, Calif.).

Detail Description Paragraph:
[0063] The effect of thioredoxin on constitutive NF-.kappa.B in AGS cells was examined. AGS cells were treated as described above with different concentrations of Trx (0.1 g/ml, 1.0 .mu.g/ml, 10 .mu.g/ml, 20 .mu.g/ml and 50 .mu.g/ml) for 2 hours. A positive control comprising HuT78 cells was used. Hut78 cells have high constitutive levels of NF-.kappa.B. The samples were analysed by EMSA and the results are shown in FIG. 1. Lane 1(C) represents a control of untreated resting AGS cells. The level of NF-.kappa.B activity decreases as the concentration of Trx increase to 20 .mu.g/ml. At 50 .mu.g Trx/ml NF-.kappa.B activity appears to increase. Using elevated extracellular amounts of thioredoxin was inimical to cell viability as judged by phase contrast microscopy and by staining cells with

ethidium bromide/acradine orange. The increase in NF-.kappa.B DNA-binding activity in this instance is likely due to stresses imposed on the cells as a consequence of exposure to elevated amounts (>20 .mu.g/ml) of thioredoxin.

Detail Description Paragraph:
[0064] The inhibition of NF-.kappa.B by Trx over time in AGS cells was examined by pre-incubating AGS cells as described above with Trx (10 .mu.g/ml) for different time period (0 mins, 15 mins, 30 mins, 60 mins, 120 mins and 240 mins) After treatment with Trx the cells were stimulated for 2 hrs with H. pylori (6.times.10.sup.8 cfU/ml). Nuclear extracts were prepared and analysed for NF-.kappa.B DNA-binding activity by EMSA. The results are shown in FIG. 2 where it can be seen that AGS cells must be exposed to Trx for at least 30 min prior to stimulation with H. pylori to block H. pylori-induced NF-.kappa.B DNA-binding activity. Control untreated AGS cells are shown in lane 1 and H. pylori treated AGS cells are shown in lanes 2-7.

Detail Description Paragraph:
[0065] The dose-dependent effect of Trx on H. pylori-induced NF-.kappa.B activation is shown in FIG. 3. AGS cells were treated for 2 hrs with increasing amounts of Trx (0.1 .mu.g/ml, 0.5 .mu.g/ml, 1.0 .mu.g/ml, 5.0 .mu.g/ml, 10 .mu.g/ml and 20 .mu.g/ml). After treatment the cells were stimulated with H. pylori (6.times.10.sup.8 cfu/ml) for a further 2 hrs and nuclear extracts were prepared and NF-.kappa.B DNA-binding activity was analysed by EMSA. FIG. 3 shows that the DNA-binding activity of NF-.kappa.B decreased when the cells were pretreated with increasing amounts of Trx. Lane C shows the resting levels of NF-.kappa.B in untreated resting AGS cells.

Detail Description Paragraph:
[0066] The effect of thioredoxin on NF-.kappa.B DNA-binding activity in response to stimulation by cytokines and mitogens is shown in FIG. 4. AGS cells were pre-treated with Trx (10 ug/ml) for 2 hrs and then stimulated with TNF.alpha. (20 ng/ml), IL-1.beta. (10 ng/ml) or PMA (20 ng/ml) for an additional 2 hrs. Nuclear extracts were prepared and NF-.kappa.B-DNA-binding activity was analysed by EMSA.

Detail Description Paragraph:
[0068] The inhibition of H. pylori-induced NF-.kappa.B by Trx was examined with the results shown in FIG. 5. AGS cells were co-cultured with H. pylori (6.times.10.sup.8 cfu/ml) to induce NF-.kappa.B activation (lane H. pylori). Subsequent to the activation of NF-.kappa.B, exogenous Trx (10 .mu.g/ml or 20 .mu.g/ml) was added to the stimulated cells (lanes+Trx (10) and +Trx (20), respectively). Nuclear extracts were prepared as described above and analysed for NF-.kappa.B DNA-binding activity by EMSA. Control untreated AGS cells are shown in lane C.

Detail Description Paragraph:
[0069] FIG. 5 shows that the NF-.kappa.B DNA-binding activity in cells stimulated by H. pylori could be reversed by the subsequent addition of Trx.

Detail Description Paragraph:
[0071] The results indicate that H. pylori Trx interacts specifically with target proteins in AGS cells.

Detail Description Paragraph:
[0072] FIG. 7. Shows the effect of Trx on CD44 and ICAM-1 expression in AGS cells. Panels A-D show the results of FACScan analyses of AGS cells (5.times.10.sup.5 cells/ml) treated with or without Trx (10 .mu.g/ml) for 24 hrs prior to staining with FITC-conjugated anti-CD44 mAb (L3D.1) (panels A, B) or anti-ICAM-1 (panels C, D) or FITC-labelled isotype matched control (anti-IE; unshaded peaks). Panels E-H show the effect of Trx on H. pylori-induced CD44 and ICAM-1 expression on AGS cells. cells. AGS cells were pre-treated with Trx (10 .mu.g/ml) for 24 hrs prior to co-

incubation with H. pylori (8.times.10.sup.6 cfu/ml) for a further 24 hrs. Cells were were stained with the same antibodies described above.

Detail Description Paragraph:
[0073] The results show that transactivation of the NFkB responsive genes encoding CD44 and ICAM-1 is down-regulated by H. pylori Trx as is the inducible expression of these adhesion molecules.

CLAIMS:

1. A H. pylori protein or derivative or fragment or mutant or variant thereof capable of inhibiting the activation of NF-.kappa.B.

2. A H. pylori protein as claimed in claim 1 wherein the protein is a thioredoxin or or derivative or fragment or mutant or variant thereof.

3. A H. pylori protein as claimed in claim 1 wherein the protein has the following amino acid sequence:

5 MSHYIELTEE NFESTIKKGV ALVDFWAPWC GPCKMLSPVI DELASEYEGK AKICKVNTDE QEELSAKFGI RSIPTLLFTK DGEVVHQLVG VQTKVALKEQ LNKLLG

4. A thioredoxin or derivative or fragment or mutant or variant thereof containing the redox active peptide sequence CGPC.

5. Prokaryotic or eukaryotic thioredoxins having potent immune-suppressive effects.

6. Polypeptides containing the redox active peptide sequence CGPC.

7. A H. pylori protein having the following amino acid sequence:

6 MSHYIELTEE NFESTIKKGV ALVDFWAPWC GPCKMLSPVI DELASEYEGK AKICKVNTDE QEELSAKFGI RSIPTLLFTK DGEVVHQLVG VQTKVALKEQ LNKLLG

9. Use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof as claimed in claim 1 in the prevention and/or treatment of inflammation.

10. Use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof as claimed in claim 9 in the prevention and/or treatment of inflammatory bowel disease.

11. Use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof as claimed in claim 9 in the prevention and/or treatment of rheumatoid/autoimmune arthritis.

12. Use of a H. pylori thioredoxin protein or derivative or fragment or variant thereof as claimed in claim 9 in the prevention and/or treatment of any chronic disease wherein NF-.kappa.B is transcriptionally activated.

14. Use of a H. pylori thioredoxin protein or derivative or fragment or mutant or variant thereof as claimed in any preceding claim in soft tissue injury.

15. A H. pylori thioredoxin protein or derivative or fragment or mutant or variant thereof as claimed in claim 1 for use in the preparation of a medicament for the treatment and/or prophylaxis of any chronic disease wherein NF-.kappa.B is transcriptionally activated.

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L8: Entry 4 of 30 File: PGPB Jul 15, 2004

DOCUMENT-IDENTIFIER: US 20040138187 A1
TITLE: Therapeutic treatment methods

Summary of Invention Paragraph:
[0406] Exemplary conditions where an immune imbalance or an excessive Th1 immune response is involved include autoimmune diseases such as multiple sclerosis, Crohn's disease (regional enteritis), ulcerative colitis, inflammatory bowel disease, rheumatoid arthritis, reactive arthritis, acute allograft rejection, sarcoidosis, type 1 diabetes mellitus, Helicobacter pylori associated peptic ulcer, graft versus host disease and Hashimotos' thyroiditis. Because these conditions are associated with a similar type immune dysfunction, a F1C can be effectively used to prevent or treat these conditions or to treat or ameliorate one or more symptoms associated therewith. Thus, in some embodiments, an unwanted or excessive Th1 response is present and amelioration of one or more symptoms associated with this condition is accomplished by administering an effective amount of a F1C according to the methods described herein, e.g., F1C is administered using a formulation and a route of administration essentially as described herein on an intermittent or a daily basis. In other embodiments, an deficient Th1 response is enhanced, which is optionally observed as a detectable increase in one or more of IFN.gamma., IL-2, IL-12 or IL-18 in Th1 cells or in accessory cells such as a dendritic cell or macrophage. In all of the conditions where an insufficient or excess Th1, Th2, Tc1 or Tc2 response is present, amelioration of one or more symptoms associated with the condition is accomplished by administering an effective amount of a F1C according to the methods described herein.

Summary of Invention Paragraph:
[0467] In some of these embodimants, the subject's hyperproliferation or malignant condition may be associated with or caused by one or more pathogens. Such conditions include hepatocellular carcinoma associated with HCV or HBV, Kaposi's sarcoma associated with HIV-1 or HIV-2, T cell leukemia associated with HTLV I, Burkitt's lymphoma associated with Epstein-Barr virus or papillomas or carcinoma associated with papilloma viruses (e.g., human HPV 6, HPV 11, HPV 16, HPV 18, HPV 31, HPV 45) or gastric adenocarcinoma, gastric MALT lymphoma or gastric inflammation associated with Helicobacter pylori, lactobacillus, enterobacter, staphylococcus or propionibacteria infection.

Summary of Invention Paragraph:
[0493] A F1C can be used to inhibit or ameliorate one or more inappropriate immune responses or their symptoms in autoimmunity, inflammation, allergy or related conditions. The effects of the F1Cs include detectably ameliorating one or more of (1) the proliferation, differentiation or chemotaxis of T cells, (2) reducing unwanted cytotoxic T cell responses, (3) reducing unwanted autoantibody or other antibody synthesis, e.g., an unwanted IgA, IgE, IgG or IgM, in allergy, asthma or another autoimmune or inflammation condition, (4) inhibiting the development, proliferation or unwanted activity of autoreactive T or B cells, (5) altering the expression of one or more cytokines, interleukins or cell surface antigens, e.g., a cytokine, interleukin or cell surface antigen described herein (decreasing IL-8 in an autoimmune condition, decreasing the level of acute phase proteins such as C reactive protein or fibrinogen in inflammation conditions, (6) decreasing

eosinophilia in allergy conditions, (7) detectably decreasing the level or activity of one or more of ICAM-1, IL-1.alpha., IL-1.beta., TNF.alpha., IL-6 or IL-8 in, e.g., inflammation conditions or in autoimmune conditions such as an arthritis or a myocarditis condition such as osteoarthritis, rheumatoid arthritis, toxic myocarditis, indurative myocarditis or idiopathic myocarditis, (8) decreasing the level or biological activity of one or more of anti-islet antibody, TNF, IFN-.gamma., IL-1, an arthritis symptom(s), nephritis, skin rash, photosensitivity, headache frequency or pain, migraine frequency or pain, abdominal pain, nausea or anti-DNA antibodies in , e.g., insulin dependent diabetes mellitus or an autoimmune or inflammation condition such as systemic lupus erythematosus, rheumatoid arthritis arthritis or Crohn's disease, (9) reducing induction of arachidonic acid metabolism or reducing eicosanoid metabolites such as thromboxanes or prostaglandins in, e.g., inflammation, asthma or allergy, (10) reducing IL-4, IL-8 or IL-10 synthesis, levels levels or activity in, e.g., allergy or inflammation such as idiopathic pulmonary fibrosis or allergic asthma or (11) reducing or interfering with neutrophil chemotaxis by, e.g., reducing thioredoxin release from affected cells in conditions such as cancer, infections, inflammation or autoimmunity.

Summary of Invention Paragraph:
[0578] An aspect of F1C biological activity is their capacity to modulate the cpacity of cells or tissues described herein to express one or more enzymes that mediate phase 11 detoxification and reduction of damaging or reactive species such as xenobiotics, including electrophiles and chemical carcinogens, and superoxide radicals or hydrogen peroxide. Modulation of these genes is mediated by one or more transcription factors or complexes of factors that include bZip transcription factors such as Nrf2 (NF-E2 related factor 2, Unigene symbol Nfe2L2) and Maf proteins such as MafG, MafK or MafF. These factors bind to cis-elements such as EpRE (electrophile response element) or ARE (antioxident response element). EpRE and/or ARE elements present in the promoters of phase II detoxification enzymes including NAD(P)H:quinine oxidoreductase-1 (NQO1) and glutathione-S-transferase (GST) as well as cellular defensive enzymes such as thioredoxins, heme oxygenase 1 (HO 1, or HMOX1), the catalytic and regulatory subunit .gamma.-glutamylcycteine syhthetase (.gamma.GCS or GCLM) and and xCT (SLC7A11), a subunit of the cystine/glutamate exchange transporter. EpRE and ARE mediate upregulation of these genes following exposure of the cells to many xenobiotics. In situations where enhanced expression of these genes or transcription factors is desirable, the F1C upregulate the activity or levels of one or more of these factors and/or enzymes.

Summary of Invention Paragraph:
[0579] Thus, in some embodiments the F1C are used to modulate the level or activity of one or more of Nrf2, a thioredoxin, NQO1, GST, HO 1, the catalytic subunit of .gamma.GCS, the regulatory subunit of .gamma.GCS and xCT in cells or tissues that are exposed to a F1C. In some embodiments, the cells or tissues are treated with a F1C when an unwanted acute or chronic condition such as toxin exposure or elevated oxidative stress is present in the cells or tissues. Such conditions can occur, e.g., as described elsewhere herein, including in acute or chronic pathological inflammation conditions, acute or chronic infections and trauma conditions. The effect of the F1Cs is restoration of normal expression or establishment of desired levels of expression of one or more of these transcription factors or enzymes, e.g., decreased expression in situations where chronic over-expression occurs. Thus, the F1C can be used to modulate these or other genes described herein, e.g., to decrease expression or mRNA levels or protein levels of one or more of these or other genes in clinical conditions where excess or unwanted expression or levels of the gene is associated with establishment, maintenance, severity or progression of the clinical condition resulting in clincal improvement in the disease or an unwanted symptom.

Summary of Invention Paragraph:
[0753] 123. The method of embodiment 122 wherein the compound modulates the level or activity of a transcription factor or enzyme selected from one or more of Nrf2,

a Maf protein, a thioredoxin, NQO1, GST, HO 1, SOD2, the catalytic subunit of .gamma.GCS, the regulatory subunit of .gamma.GCS and xCT.

Summary of Invention Paragraph:
[0756] 126. The method of embodiment 122, 123, 124 or 125 wherein the levels or activity of one, two or more of Nrf2, a Maf protein, a thioredoxin, NQO1, GST, HO 1, the catalytic subunit of .gamma.GCS, the regulatory subunit of .gamma.GCS and xCT is increased.

Detail Description Paragraph:
[0850] Exemplary genes of interest that can be analyzed by this or a similar protocol include 1, 2, 3, 4, 5, 6 or more of iNOS (inducible nitric oxide synthase), eNOS (constitutive nitric oxide synthase), COX-2 (cycloxygenase-2, PGE2 synthase), I.kappa.B.beta., TNF.alpha., IL-1.beta., IL-1Ra (interleukin 1 receptor antagonist), NF.kappa.B1 (p105), NF.kappa.B2 (p49/p100), IL-6, MCP-1 (monocyte chemoattractant prtein-1 or CCL2), MIP-2 (macrophage inflammatory protein-2), MMP9 (matrix metalloproteinase 9), gelatinase B, HO-1 (heme oxygenase 1), HIF1.alpha. (hypoxia inducible factor 1, alpha subunit), GCLC (gamma glutamylcycteine synthetase catalytic (heavy) subunit or .gamma.GCS-hs), GCLM (gamma glutamylcycteine synthetase modifier (light) subunit or .gamma.GCS-ls), xCT (cystine/glutamate exchange transporter), NQO1 (NAD(P)H: quinone oxidoreductase 1), TXNRD1 (thioredoxin reduatase 1), EBBP (estrogen responsive B-box protein), CYP1A1 (cytochrome P450), CD36 (SR-B), SR-A (scavenger receptor A or Msr1), ABCA1 (ATP-binding cassette transporter A1), ABCG1 (ATP-binding cassette transporter G1), LDLR (low-density lipoprotein receptor), NR1H3 (nuclear receptor 1 H3 or LXR.alpha.), NR1C3 (nuclear receptor 1C3 or PPAR.gamma.), SCD-1 (stearoyl-CoA desaturase 1) and NR4A1 (nuclear receptor 4A1 or Nur77). F1C that can be characterized in this manner include the F1Cs in the compound groups described above, e.g., one or more of 16.alpha.-bromoepiandrosterone, 3.beta.,16.alpha.-dihydroxyandrostane-17-- one, 3.beta.,16.alpha.,17.beta.-trihydroxyandrostane, 3.alpha.,16.alpha.,17.beta.-trihydroxyandrostane, 3.beta.,17.beta.-dihydr- oxy-16.alpha.-fluoroandrost-5-ene, 3.beta.,17.beta.-dihydroxy-16.alpha.-fl- uoroandrost-1,5-diene, 3.beta.-hydroxy-17.beta.-aminoandrost-5-ene, 3.beta.,7.beta.-dihydroxy-17.beta.-aminoandrost-5-ene, 3.beta.-hydroxy-7-oxo-17.beta.-aminoandrost-5-ene, 3.alpha.-hydroxy-17.beta.-aminoandrost-5-ene, 3.beta.-hydroxy-17.beta.-am- inoandrost-1,5-ene, 3.alpha.-hydroxy-17.beta.-aminoandrost-1,5-diene, 3.beta.-hydroxy-16.alpha.-fluoro-17.beta.-aminoandrost-5-ene or 3.beta.-hydroxy-16.alpha.-fluoro-17.beta.-aminoandrost-1,5-diene.

CLAIMS:

27. A method to modulate the expression in a cell of the level of or an activity of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more gene products or gene transcripts in the cell, comprising contacting an effective amount of the compound with the cell under suitable conditions and for a sufficient time to detectably modulate the activity or level of the genes, or gene products in the cell, wherein the compound is a compound of any of embodiments 1-9 and the gene products or gene transcripts are selected from USF1, c-Fos, EGR1, Cul1, RIPK2, I.kappa.Ba, I.kappa.BKb, NF-.kappa.B1 p50, FCAR, c-Fos/C/EBP.beta., RANTES, ICAM1, TSG (TNFAIP6), IL-2 receptor .alpha., GRO2, GRO3, HO1, Jun B, c-Fos/JunB complex, JunB/ATF3 complex, c-Jun, c-Fos/c-Jun complex, ATF-3, MMP1, TSG-6 (TNFAIP3), AP-1, EGR1, TGF.beta., ATF-3/c-Jun complex, c-Fos, MMP3, IL-8, STAT5A, STAT5B, CDKN1A, IFN.gamma. receptor 2 (IFN.gamma.R2), T-bet, C reactive protein, immunoglobulin E, an AP-1family protein, GATA-3, Jak2, Tyk2, stat1, stat3, stat4, stat5, stat6, MIP-1.alpha., MIP-2, IP-10, MCP-1, TNF-.alpha., TNF-.beta., LT-.beta., IFN-.alpha., IFN-.beta., TGF-.beta.1, NF-.kappa.B, IL-1.alpha., IL-1.beta., IL-4, IL-6, IL-10, IL-12 receptor .beta.1, IL-12p35, IL-12p40, IL-23, IL-23 receptor, Nrf2, a Maf protein, a thioredoxin, NQO1, GST, HO 1, SOD2, the catalytic subunit of .gamma.GCS, the regulatory subunit of .gamma.GCS and xCT.

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L8: Entry 4 of 30 File: PGPB Jul 15, 2004

PGPUB-DOCUMENT-NUMBER: 20040138187
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040138187 A1

TITLE: Therapeutic treatment methods

PUBLICATION-DATE: July 15, 2004

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US-CL-CURRENT: 514/169

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L8: Entry 5 of 30 File: PGPB May 6, 2004

DOCUMENT-IDENTIFIER: US 20040086896 A1
TITLE: Polynucleotides and polypeptides associated with the NF-kB pathway

Abstract Paragraph:
The present invention provides polynucleotides encoding NF-kB-associated polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these NF-kB-associated polypeptides to the diagnosis, treatment, and/or and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

Detail Description Paragraph:
[0794] Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein, the addition of epitope tagged peptide fragments (e.g., FLAG, HA, GST, thioredoxin, maltose binding protein, etc.), attachment of affinity tags such as biotin and/or streptavidin, the covalent attachment of chemical moieties to the amino acid backbone, N- or C-terminal processing of the polypeptides ends (e.g., proteolytic processing), deletion of the N-terminal methionine residue, etc.

Detail Description Paragraph:
[0915] Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat. Res. 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem. Biol. Interact. April 24;1 11-112:23-34 (1998), J Mol Med.76(6):402-12 (1998), Int. J. Tissue React. 20(l):3-15 (1998), which are all hereby incorporated by reference).

Detail Description Paragraph:

[0948] Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated, prevented, and/or diagnosed by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia (e.g., Borrelia burgdorferi), Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, E. coli (e.g., Enterotoxigenic E. coli and Enterohemorrhagic E. coli), Enterobacteriaceae (Klebsiella, Salmonella (e.g., Salmonella typhi, and Salmonella paratyphi), Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Mycobacterium leprae, Vibrio cholerae, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Meisseria meningitidis, Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus (e.g., Heamophilus influenza type B), Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, Shigella spp., Staphylococcal, Meningiococcal, Pneumococcal and Streptococcal (e.g., Streptococcus pneumoniae and Group B Streptococcus). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis (e.g., mengitis types A and B), Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat, prevent, and/or diagnose any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, agonists or antagonists of the invention are used to treat, prevent, and/or diagnose: tetanus, Diptheria, botulism, and/or meningitis type B.

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L8: Entry 7 of 30 File: PGPB Dec 4, 2003

DOCUMENT-IDENTIFIER: US 20030224458 A1
TITLE: Novel human G-protein coupled receptor, HGPRBMY23, expressed highly in kidney kidney

Detail Description Paragraph:
[0482] Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of prokaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein, the addition of epitope tagged peptide fragments (e.g., FLAG, HA, GST, thioredoxin, maltose binding protein, etc.), attachment of affinity tags such as biotin and/or streptavidin, the covalent attachment of chemical moieties to the amino acid backbone, N- or C-terminal processing of the polypeptides ends (e.g., proteolytic processing), deletion of the N-terminal methionine residue, etc.

Detail Description Paragraph:
[0603] Polypeptides, including protein fusions, of the present invention, or fragments thereof may be useful in inhibiting proliferative cells or tissues through the induction of apoptosis. Said polypeptides may act either directly, or indirectly to induce apoptosis of proliferative cells and tissues, for example in the activation of a death-domain receptor, such as tumor necrosis factor (TNF) receptor-1, CD95 (Fas/APO-1), TNF-receptor-related apoptosis-mediated protein (TRAMP) and TNF-related apoptosis-inducing ligand (TRAIL) receptor-1 and -2 (See Schulze-Osthoff K, et al., Eur J Biochem 254(3):439-59 (1998), which is hereby incorporated by reference). Moreover, in another preferred embodiment of the present invention, said polypeptides may induce apoptosis through other mechanisms, such as in the activation of other proteins which will activate apoptosis, or through stimulating the expression of said proteins, either alone or in combination with small molecule drugs or adjuvants, such as apoptonin, galectins, thioredoxins, antiinflammatory proteins (See for example, Mutat. Res. 400(1-2):447-55 (1998), Med Hypotheses.50(5):423-33 (1998), Chem. Biol. Interact. Apr 24;111-112:23-34 (1998), J Mol Med. 76(6):402-12 (1998), Int. J. Tissue React. 20(1):3-15 (1998), which are all hereby incorporated by reference).

Detail Description Paragraph:
[0620] Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated, prevented, and/or diagnosed by a polynucleotide or polypeptide and/or agonist or antagonist of the present invention include, but not limited to, include, but not limited to, the following Gram-Negative and Gram-positive bacteria and bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Cryptococcus neoformans, Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia (e.g., Borrelia burgdorferi), Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, E. coli (e.g., Enterotoxigenic E. coli and Enterohemorrhagic E. coli), Enterobacteriaceae (Klebsiella, Salmonella

(e.g., Salmonella typhi, and Salmonella paratyphi), Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Mycobacterium leprae, Vibrio cholerae, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Meisseria meningitidis, Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus (e.g., Heamophilus influenza type B), Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, Shigella spp., Staphylococcal, Meningiococcal, Pneumococcal and Streptococcal (e.g., Streptococcus pneumoniae and Group B Streptococcus). These bacterial or fungal families can cause the following diseases or symptoms, including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis (e.g., mengitis types A and B), Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. Polynucleotides or polypeptides, agonists or antagonists of the invention, can be used to treat, prevent, and/or diagnose any of these symptoms or diseases. In specific embodiments, polynucleotides, polypeptides, agonists or antagonists of the invention are used to treat, prevent, and/or diagnose: tetanus, Diptheria, botulism, and/or meningitis type B.

CLAIMS:

17. A method for treating, or ameliorating a medical condition with the polypeptide provided as SEQ ID NO:2, or a modulator thereof, wherein the medical condition is a member of the group consisting of: a disorder related to aberrant NF-kB activity; disorders related to aberrant IkBa expression or activity; a disorder linked to aberrant DNA synthesis; a disorder related to aberrant purinergic receptor activity or expression; a renal disorder; an inflammatory disorder; an inflammatory disease where purinergic receptors, either directly or indirectly, are involved in disease progression; a neural disorder; a pulmonary disorder; disorders related to aberrant signal transduction; proliferative disorder of the colon; colon cancer; colon adenocarcinoma; disorders associated with the immune respone to tumors, particularly the response of neutrophils and/or macrophages; proliferative disorder of the breast; breast cancer; other proliferative diseases and/or disorders; female reproductive disorders; a metabolic disorders; a thyroid disorder; a disorder wherein increased NFkB expression or activity would be therapeutically beneficial; a disorder wherein decreased NFkB expression or activity would be therapeutically beneficial; a disorder wherein increased IkB expression or activity would be therapeutically beneficial; a disorder wherein decreased IkB expression or activity would be therapeutically beneficial; a disorder wherein increased apoptosis would be therapeutically beneficial; a disorder wherein decreased apoptosis would be therapeutically beneficial; healing disorder; and necrosis disorder.

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L8: Entry 10 of 30 File: PGPB Sep 4, 2003

DOCUMENT-IDENTIFIER: US 20030166192 A1
TITLE: Inhibition of interleukin-1-beta secretion by card proteins

Detail Description Paragraph:
[0147] The polypeptides that Pseudo-ICE or ICE-Like polypeptides or functional fragments thereof fused to can be full-length proteins or polypeptide fragments. Proteins commonly used in fusion protein construction include .beta.-galactosidase, .beta.-glucuronidase, green fluorescent protein (GFP), autofluorescent proteins, including blue fluorescent protein (BFP), glutathione-S-transferase (GST), luciferase, horseradish peroxidase (HRP), and chloramphenicol acetyltransferase (CAT). Additionally, epitope tags can be used in fusion protein constructions, including histidine (His) tags, FLAG tags, influenza hemagglutinin (HA) tags, Myc tags, VSV-G tags, and thioredoxin (Trx) tags. Other fusion constructions can include include maltose binding protein (MBP), S-tag, Lex a DNA binding domain (DBD) fusions, GAL4 DNA binding domain fusions, and herpes simplex virus (HSV) BP16 protein fusions.

CLAIMS:

1. An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO: 1, an immunogenic fragment of the Pseudo-ICE, or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation.

11. An isolated polypeptide comprising a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO: 1, an immunogenic fragment of the Pseudo-ICE, or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation.

13. An isolated polypeptide encoded by a nucleotide sequence at least 98% identical to SEQ ID NO: 2 and having an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation.

16. A method of transforming or transfecting a cell with a nucleic acid molecule encoding a Pseudo-ICE that has at least 80% amino acid identity to SEQ ID NO: 1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation, comprising contacting the the cell with a vector comprising the nucleic acid molecule under the control of a promoter.

43. A method of stimulating the activation of an NF-kB comprising contacting a cell expressing the NF-kB with a composition comprising the isolated polypeptide of claim claim 11 or claim 12 under conditions and for a time sufficient to permit the inhibition of the activation of the NF-kB.

44. A method of stimulating the activation of an NF-kB comprising contacting a cell expressing the NF-kB with a composition comprising the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the inhibition of the activation of the NF-kB.

45. A method of inhibiting the activation of an NF-kB comprising contacting a cell expressing the NF-kB a composition comprising a polypeptide that specifically binds to the isolated polypeptide of claim 11 or claim 12 under conditions and for a time sufficient to permit the stimulation of the activation of the NF-kB.

47. A method of inhibiting the activation of an NF-kB comprising contacting a cell expressing the NF-kB a composition comprising an antisense or ribozyme construct of the isolated nucleic acid molecule of any one of claims 1-3 under conditions and for a time sufficient to permit the stimulation of the activation of the NF-kB.

48. A method of identifying inhibitors or enhancers of Pseudo-ICE mediated NF-kB activation, comprising: a. contacting a cell transfected with an expression vector encoding Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO: 1 or a functional fragment of the Pseudo-ICE capable of stimulating NF-.kappa.B activation with a candidate inhibitor or enhancer; and b. detecting an increase or decrease in NF-kB activation in the presence of the candidate inhibitor or enhancer, wherein a decrease in NF-kB activation indicates the presence of an inhibitor and an increase in NF-kB indicates the presence of an enhancer.

50. A method of identifying a polypeptide that specifically binds to a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO: 1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation, comprising: a. contacting a sample with the Pseudo-ICE or the functional fragment under conditions that permit the formation of a complex between the Pseudo-ICE or the functional fragment thereof and the polypeptide; and b. detecting the complex and polypeptide in the complex.

56. A nucleic acid molecule comprising a first nucleic acid sequence encoding a Pseudo-ICE having at least 80% identity to SEQ ID NO: 1 or a finctional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation and a second nucleic acid sequence encoding the transcription activation domain or the DNA-binding domain of a transcription factor.

57. A method for identifying a polypeptide that specifically binds to a Pseudo-ICE having at least 80% amino acid identity to SEQ ID NO: 1 or a functional fragment of the Pseudo-ICE that has an activity selected from: specific binding to pro-caspase-1, specific binding to RICK, inhibiting induced IL-1.beta. secretion, and stimulating NF-.kappa.B activation with a yeast two-hybrid screening system, comprising transforming a yeast cell with a vector comprising the nucleic acid molecule of claim 56.

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L8: Entry 12 of 30 File: PGPB Jun 19, 2003

DOCUMENT-IDENTIFIER: US 20030113733 A1
TITLE: Gene regulator

Summary of Invention Paragraph:
[0013] Considering that NF-kappaB is thought by many to be a primary effector of disease (A. S. Baldwin, J. Clin. Invest., 2001, 107:3-6), numerous efforts are underway to develop safe inhibitors of NF-kappaB to be used in treatment of both chronic and acute disease situations. Specific inhibitors of NF-kappaB should reduce side effects associated with drugs such as NSAIDS and glucocorticoids and would offer significant potential for the treatment of a variety of human and animal diseases. Specific diseases or syndromes where patients would benefit from NF-kappaB inhibition vary widely, and range from rheumatoid artrhritis, athereosclerosis, multiple sclerosis, chronic inflammatory demyelinating polyradiculoneuritis, asthma, inflammatory bowel disease, to Helicobacter pylori-associated gastritis and other inflammatory responses, and a variety of drugs that have effects on NF-kappaB activity, such as corticosteroids, sulfasalazine, 5-aminosalicylic acid, aspirin, tepoxalin, leflunomide, curcumin, antioxidants and proteasome inhibitors. These drugs are considered to be non-specific and often only applicable in high concentrations that may end up toxic for the individual treated.

CLAIMS:

22. A modulator of NF-kappaB/Rel protein activation comprising a signalling molecule molecule according to anyone of claims 18 to 21.

24. Use according to claim 23 for the modulation of gene expression by inhibiting NF-kappaB/Rel protein activation.

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L8: Entry 14 of 30 File: PGPB May 1, 2003

DOCUMENT-IDENTIFIER: US 20030083241 A1
TITLE: Use of somatostatin receptor agonists in the treatment of human disorders of sleep hypoxia and oxygen deprivation

Detail Description Paragraph:
[0246] Ludtke, F. E., Maierhof, S., Kohler, H., Bauer, F. E., Tegeler, R., Schauer, A., and Lepsien, G., Helicobacter pylori colonization in surgical patients, Chirurg. Chirurg. 62: 732-8., 1991.

CLAIMS:

61. The method of preventing or treating gastroesophageal reflux disease (GERD), asthma-associated gastroesophageal reflux (GER), GER-associated asthma and asthma, or related disorders, which method comprises administering a composition comprising an effective amount of a somatostatin receptor agonist sufficient to inhibit the activation of NF-kappaB and c-fos/AP-1 nuclear transcription factors to a human patient in need thereof.

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L8: Entry 17 of 30 File: PGPB Apr 3, 2003

DOCUMENT-IDENTIFIER: US 20030064913 A1
TITLE: Treatment and prevention of mucositis in cancer patients

Abstract Paragraph:
The invention features a method for the treatment or prevention of mucositis in an individual undergoing or preparing to undergo cancer treatment. The method includes administering a therapeutically effective amount of an inhibitor of NF-.kappa.B to an individual undergoing or preparing to undergo a treatment for cancer. In certain embodiments, the inhibitor is a compound having the formula: 1

Detail Description Paragraph:
[0186] 120. Jin D-Y, Chae H Z, Rhee S G and Jeang K-T (1997) Regulatory role for a novel human thioredoxin peroxidase in NF-.kappa.B activation. Journal of Biological Chemistry 272 30952-30961.

CLAIMS:

1. A method for the treatment or prevention of mucositis comprising administering a therapeutically effective amount of an inhibitor of NF-.kappa.B to an individual undergoing or preparing to undergo a treatment for cancer.

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L8: Entry 22 of 30 File: USPT Jul 23, 2002

DOCUMENT-IDENTIFIER: US 6423687 B1
TITLE: Pharmaceutical preparations of glutathione and methods of administration thereof

Other Reference Publication (95):
Holmgren, "Thioredoxin and glutaredoxin", J. Biol. Chem. 264, 13963-13966 1989.

Other Reference Publication (97):
Matthews, et al., "Thioredoxin regulates the DNA binding activity of NF-kB by reduction . . . ", Nucleic Acids Research, 20 (15): 3821-3830 1992.

Other Reference Publication (100):
Qin, et al., "Solution structure of human thioredoxin in a mixed disulfide intermediate complex . . . ", Structure, 15:3, 289-297 1995.

Other Reference Publication (101):
Qin, et al., "The Solution structure of human thioredoxin complexed with its target from Ref-1 reveals peptide chain reversal", Structure, 4(5), 613-620 1996.

Other Reference Publication (219):
Muriel, et al., "Dual regulation of heat-shock transcription factor (HSF) activation and DNA-binding activity by H202: role of thioredoxin". (1996).

Other Reference Publication (220):
Makino, et al., Cross-Talk between Endocrine Control of Stress Response and Cellular Antioxidant Defense System, Thioredoxin is a Redox-Regulating Cellular Cofactor for Glucocorticoid Hormone Action (Poster), Proceedings of 3rd Internet World Congress on Biomedical Sciences, 1996.12.9-20 Riken, Tsukuba, Japan.

Other Reference Publication (247):
Holmgren, A., 1995, "Thioredoxin structure and mechanism: conformational changes on oxidation of the active-site sulfhydryls to a disulfide", Structure 3:239-243.

Other Reference Publication (248):
Holmgren, A., 1985, "Thioredoxin", Annu. Rev. Biochem. 54:237-271.

Other Reference Publication (249):
Tagaya, et al., 1989, "ATL-derived factor (ADF), an IL-2 receptor/Tac inducer homologous to thioredoxin . . . ", EMBO J. 8:757-764.

Other Reference Publication (252):
Schenk, et al., 1994, "Distinct effects of thioredoxin and antioxidants on the activation of transcription factors NF-kB and AP-1", Proc. Natl. Acad. Sci. USA. 91:1672-1676.

Other Reference Publication (254):
Grippo, et al., 1985, "Proof that the endogenous, heat-stable glucocorticoid receptor-activating factor is thioredoxin", J. Biol. Chem. 260:93-97.

Other Reference Publication (255):
Makino, et al., Thioredoxin: a Redox-Regulating Cellular Cofactor for Glucocorticoid Glucocorticoid Hormone Action. J. Clin. Invest. (in press).

Other Reference Publication (256):
Sasada, et al., 1996, "Redox control of resistence to cis-diamminedichloroplatinum (II) (CDDP). Protective effect of human thioredoxin against CDDP-induced cytotoxicity", J. Clin. Invest. 97:2268-2276.

Other Reference Publication (260):
Matthews, et al., 1992, "Thioredoxin regulates the DNA binding activity of NF-kB by reduction of a disulphide bond involving cysteine 62", Nucleic Acids Res. 20:3821-3830.

Other Reference Publication (261):
Yokomizo, et al., 1995, "Cellular levels of thioredoxin associated with drug sensitivity to cisplatin, mitomycin C, doxorubicin, and etoposide", Cancer Res. 55:4293-4296.

Other Reference Publication (269):
Qin, et al., "Solution structure of human thioredoxin in a mixed disulfide intermediate complex with its target peptide from the transcription factor NfkB", Structure 3:289-297.

Other Reference Publication (356):
Holmgren, A., "Thioredoxin", Ann Rev Biochem 1985; 54: 237-272.

Other Reference Publication (357):
Holmgren, A., "Thioredoxin and glutaredoxin systems", J Biol Chem 1989; 264, 13963-13966.

Other Reference Publication (392):
Okamoto, et al., "Human thioredoxin/adult T cell leukemia-derived factor activates the enhancer binding protein . . . ", Int Immunol 1992; 4: 811-819.

Other Reference Publication (393):
Hayashi, et al., "Oxidoreductive regulation of nuclear factor kappa B. Involvement of a cellular reducing catalyst thioredoxin", J Biol Chem 1993B; 268: 11380-11388.

Other Reference Publication (394):
Tagaya, et al., "ATL-derived factor (ADF), an IL-2 receptor/Tac inducer homologous to thioredoxin . . . ", EMBO J 1989; 8: 757-764.

Other Reference Publication (398):
Matthews et al., "Thioredoxin regulates the DNA binding activity of NF-kappa B by reduction of a disulfide bond involving cystein 62", Nucleic Acids Res 1992; 20, 3821-3830.

Other Reference Publication (401):
Qin, et al., "Solution structure of human thioredoxin in a mixed disulfide intermediate complex with its target peptide . . . ", Science 1995; 3: 289-297.

Other Reference Publication (549):
Junji, Y., et al., Redox control of Thioredoxin (TRX) on the cytotoxic/death signal

CLAIMS:

3. The method according to claim 1, wherein the glutathione blocks induction of NF-.kappa.B transcription factor.

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First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

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L8: Entry 23 of 30 File: USPT Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837224 A
** See image for Certificate of Correction **
TITLE: Method of inhibiting photoaging of skin

Abstract Text (1):
Photoaging of undamaged skin due to UVB irradiation exposure is inhibited by administering an agent that inhibits (1) the activity of UVB irradiation inducible MMPs in the skin, (2) one or both of the transcription factors AP-1 and NF-.kappa.B or (3) at least one of the GTP binding proteins or kinases involved in the activation and/or production of jun or fos proteins, which comprise AP-1, to the skin prior to such exposure.

Other Reference Publication (78):
Schenk et al., "Distinct effects of thioredoxin and antioxidants on the activation of transcription factors NF-kB and APP-1" Proc. Natl. Acad. Sci. USA (1994) 91:1672-1676.

CLAIMS:

4. The method of claim 1 wherein the inhibitor inhibits the activity of at least one one of AP-1 and NF-.kappa.B.

8. The method of claim 4 wherein the inhibitor inhibits NF-.kappa.B and is a glucocorticoid, aspirin or E5510.

16. The method of claim 11, wherein the inhibitor inhibits the activity of at least one of AP-1 and NF-.kappa.B.

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L8: Entry 26 of 30 File: DWPI Nov 27, 2003

DERWENT-ACC-NO: 2004-061982
DERWENT-WEEK: 200406

TITLE: Identifying compounds that modulate lipopolysaccharide-mediated activation of of NF-kB or JNK kinase activity, useful for treating bacterial infections, comprises comprises exposing a cell to a compound that modulates the activity of CARD-4

PATENT-ASSIGNEE:

ASSIGNEE	CODE
INST PASTEUR	INSP

PRIORITY-DATA: 2003US-0352381 (January 27, 2003), 2002US-0154485 (May 22, 2002)

Search Selected Search ALL Clear

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2003097684 A2	November 27, 2003	E	104	C07K014/47

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO2003097684A2	May 22, 2003	2003WO-IB02597	

INT-CL (IPC): C07 K 14/47

ABSTRACTED-PUB-NO: WO2003097684A
BASIC-ABSTRACT:

NOVELTY - Identifying a candidate compound that modulates lipopolysaccharide (LPS)-mediated activation of NF-kB or JNK kinase activity comprising exposing a cell to a compound that modulates the expression or activity of CARD-4, is new.

DETAILED DESCRIPTION - Identifying a candidate compound that modulates lipopolysaccharide (LPS)-mediated activation of NF-kB or JNK kinase activity comprising:

(a) providing a cell that harbors LPS and expresses a polypeptide comprising a caspase recruitment domain (CARD), nucleotide binding site (NBS) or leucine rich repeat (LRR) domain of CARD-4;

(b) exposing the cell to a test compound; and

(c) measuring NF-kB activation or JNK kinase activity in the cell, where altered NF-kB activation or JNK kinase activity in the presence of the test compound compared to NF-kB activation or JNK kinase activity in the absence of the test compound indicates that the test compound is a candidate compound that modulates LPS-mediated activation of NF-kB or JNK kinase activity.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying a candidate compound that modulates LPS-induced immune response, comprising:

(a) providing a cell that expresses a polypeptide comprising a CARD, NBS or LRR domain of CARD-4;

(b) introducing LPS into the cell;

(c) exposing the cell to a test compound; and

(d) measuring oligomerization of the polypeptide in the cell, where an altered oligomerization of the polypeptide in the presence of the test compound compared to oligomerization of the polypeptide in the absence of the test compound indicates that the test compound is a candidate compound for modulating an LPS-induced immune response;

(2) modulating LPS-induced activation of NF-kB or JNK, comprising providing a cell that harbors intracellular LPS, and contacting the cell with a compound that modulates expression or activity of CARD-4 in an amount sufficient to modulate LPS-induced activation of NF-kB or JNK in the cell;

(3) modulating an LPS-induced immune response in an individual, comprising selecting an individual comprising cells harboring intracellular LPS, and administering to the individual a compound that modulates expression or activity of CARD-4 in an amount sufficient to modulate an LPS-induced immune response in the individual;

(4) treating or preventing a bacterial infection, comprising selecting an individual having or at risk of having a bacterial infection, and administering to the individual a compound that modulates expression or activity of CARD-4 in an amount sufficient to treat or prevent the bacterial infection; and

(5) a mouse whose genome comprises a disruption in an endogenous CARD-4 gene, where the disruption results in decreased expression or a lack of expression of the endogenous CARD-4 gene, thus, causing a decreased ability of the mouse to clear a Salmonella typhimurium or Helicobacter pylori infection.

ACTIVITY - Antibacterial; Antiinflammatory; Auditory; Respiratory-Gen.; Immunosuppressive; Cytostatic; Antiarthritic; Dermatological; Nephrotropic; Anti-HIV; Neuroprotective; Nootropic; Antiparkinsonian; Antianemic; Antithyroid; Antiallergic.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The method is useful in screening for modulators of LPS-induced cell signaling signaling pathways, in modulating LPS-induced cell signaling pathways, or in diagnosing, preventing or treating bacterial infections such as those caused by S. flexneri, S. typhimurium or H. pylori, or disorders of bacterial origin, such as sinusitis, acute otitis media, chronic obstructive pulmonary disease, inflammatory bowel disease, appendicitis or septic shock. These may also be used for diagnosing, preventing or treating other disorders such as cancer, arthritis, systemic lupus erythematosus, glomerulonephritis, HIV, Alzheimer's disease, Parkinson's disease, anemia, Grave's disease or allergies. The proteins, nucleic acid molecules or antibodies may also be used in chromosomal mapping, tissue typing, forensic biology or pharmacogenomics.

CHOSEN-DRAWING: Dwg.0/7

TITLE-TERMS: IDENTIFY COMPOUND MODULATE MEDIATOR ACTIVATE KINASE ACTIVE USEFUL TREAT BACTERIA INFECT COMPRISE EXPOSE CELL COMPOUND MODULATE ACTIVE CARD

DERWENT-CLASS: B04 D16

CPI-CODES: B04-F01; B04-F02A0E; B04-P01A0E; B11-C08E1; B12-K04A; B12-K04E; B14-A01; B14-A01A8; B14-A02B1; B14-C09; B14-E10C; B14-F03; B14-G01B; B14-G02A; B14-H01; B14-H01B; B14-J01A3; B14-J01A4; B14-K01; B14-N02; B14-N04; B14-N10; B14-N11; B14-N17C; B14-S06; D05-H08; D05-H09; D05-H14B2; D05-H16;

CHEMICAL-CODES:

Chemical Indexing M6 *01*
Fragmentation Code
M905 P210 P220 P420 P421 P431 P444 P446 P624 P625
P631 P633 P723 P731 P812 P820 P831 P921 P924 P943
Q233 Q505 R515 R521 R614 R627 R633

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2004-025301

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L15: Entry 2 of 12 File: PGPB Jun 10, 2004

DOCUMENT-IDENTIFIER: US 20040109870 A1
TITLE: Therapeutic agent for acute hepatitis and chronic hepatitis including hepatic hepatic fibrosis and cirrhosis

CLAIMS:

5. A method for treating hepatic disease comprising administering an effective amount of one or more polypeptide(s) belonging to the thioredoxin family to a patient in need of such treatment, wherein the hepatic disease is acute hepatitis, chronic hepatitis, chronic hepatic fibrosis or hepatic cirrhosis.

6. The method according to claim 5, wherein about 50 to about 500 mg of thioredoxin is administered to an adult per day.

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L15: Entry 5 of 12 File: PGPB Dec 25, 2003

DOCUMENT-IDENTIFIER: US 20030235588 A1
TITLE: Method of treating TRX mediated diseases

CLAIMS:

1. A method of treating a thioredoxin (TRX)-mediated disease in a subject in need thereof, comprising the step of administering to said subject a therapeutically effective amount of a histone deacetylase (HDAC) inhibitor, or pharmaceutically acceptable salts or hydrates thereof.

31. A method of modulating the level or activity of thioredoxin (TRX) in a subject, comprising the step of administering to said subject a histone deacetylase (HDAC) inhibitor, or pharmaceutically acceptable salts or hydrates thereof, in an amount effective to modulate the level or activity of TRX in said subject.

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L15: Entry 6 of 12 File: PGPB Nov 20, 2003

DOCUMENT-IDENTIFIER: US 20030215542 A1
TITLE: Use of thiol redox proteins for reducing protein intramolecular disulfide bonds, for improving the quality of cereal products, dough and baked goods and for inactivating snake, bee and scorpion toxins

CLAIMS:

118. A method of treating snake venom neurotoxicity in an individual comprising administering, to an individual suffering from snake venom neurotoxicity, amounts of of NADP-thioredoxin reductase, NADPH or an NADPH generator system and a thioredoxin effective for reducing or alleviating said snake venom neurotoxicity.

136. A method of treating bee venom toxicity in an individual comprising administering, to an individual suffering from bee venom toxicity, amounts of NADP-thioredoxin reductase, NADPH or an NADPH generator system and a thioredoxin effective for reducing or alleviating said bee venom toxicity.

137. A method of treating scorpion venom toxicity in an individual comprising administering, to an individual suffering from scorpion venom toxicity, amounts of NADP-thioredoxin reductase, NADPH or an NADPH generator system and a thioredoxin effective for reducing or alleviating said scorpion venom toxicity.

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10875226 PMID: 11006259

Lipid peroxidation and peroxynitrite in retinal ischemia-reperfusion injury.

Shibuki H; Katai N; Yodoi J; Uchida K; Yoshimura N

Department of Ophthalmology, Shinshu University School of Medicine, Matsumoto, Japan.

Investigative ophthalmology & visual science (UNITED STATES) Oct 2000, 41 (11) p3607-14, ISSN 0146-0404 Journal Code: 7703701

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

PURPOSE: To investigate whether lipid peroxides play a role in retinal cell death due to ischemia-reperfusion injury, whether recombinant human thioredoxin (rhTRX) treatment reduces production of lipid peroxides of the retina, and whether such treatment reduces the number of cells expressing c-Jun and cyclin D1. METHODS: Retinal ischemia was induced in rats by increasing the intraocular pressure to 110 mm Hg for 60 minutes. After reperfusion, immunohistochemical staining for lipid peroxide, peroxynitrite, c-Jun, and cyclin D1 and propidium iodide (PI) staining were performed on retinal sections from animals treated intravenously with and without rhTRX, a free radical scavenger. Quantitative analyses of PI-, c-Jun-, and cyclin D1-positive cells were performed after the ischemic insult. Concentration of lipid peroxides in the retina was determined by the thiobarbituric acid assay. RESULTS: Specific immunostaining for lipid peroxides was seen in the ganglion cell layer at 6 hours after reperfusion, in the inner nuclear layer at 12 hours, and in the outer nuclear layer at 48 hours. Time course studies for PI-positive cells in the three nuclear layers coincided with those of specific immunostaining for lipid peroxides. The specific immunostaining was weakened by pre- and posttreatment with 0.5 mg of rhTRX. The number of PI-, c-Jun-, and cyclin D1-positive cells and the concentration of lipid peroxides were significantly decreased by treatment with rhTRX compared with those of vehicle-treated control rats (P: < 0. 01). CONCLUSIONS: Lipid peroxides formed by free radicals may play a role in neuronal cell death in retinal ischemia-reperfusion injury.

Tags: Male; Support, Non-U.S. Gov't

Descriptors: *Lipid Peroxidation; *Lipid Peroxides--metabolism--ME; *Nitrates--metabolism--ME; *Reperfusion Injury--metabolism--ME; *Retina --metabolism--ME; *Retinal Diseases--metabolism--ME; Aldehydes--metabolism --ME; Animals; Cell Death; Cyclin D1--metabolism--ME; Fluorescent Antibody Technique, Indirect; Free Radical Scavengers--therapeutic use--TU; Propidium--metabolism--ME; Proto-Oncogene Proteins c-jun--metabolism--ME; Rats; Rats, Sprague-Dawley; Recombinant Proteins--therapeutic use--TU; Reperfusion Injury--drug therapy--DT; Reperfusion Injury--pathology--PA; Retina--pathology--PA; Retinal Diseases--drug therapy--DT; Retinal Diseases--pathology--PA; Thiobarbituric Acid Reactive Substances; **Thioredoxin** --therapeutic use--TU

10878975 PMID: 11012661

Physiological functions of thioredoxin and thioredoxin reductase.

Arner E S; Holmgren A

Medical Nobel Institute for Biochemistry, Department of Medical Biochemistry and Biophysics, Karolinska Institute, Stockholm, Sweden.

European journal of biochemistry / FEBS (GERMANY) Oct 2000, 267 (20) p6102-9, ISSN 0014-2956 Journal Code: 0107600

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Thioredoxin, thioredoxin reductase and NADPH, the thioredoxin system, is ubiquitous from Archea to man. Thioredoxins, with a dithiol/disulfide active site (**CGPC**) are the major cellular protein disulfide reductases; they therefore also serve as electron donors for enzymes such as ribonucleotide reductases, thioredoxin peroxidases (peroxiredoxins) and methionine sulfoxide reductases. Glutaredoxins catalyze glutathione-disulfide oxidoreductions overlapping the functions of thioredoxins and using electrons from NADPH via glutathione reductase. Thioredoxin isoforms are present in most organisms and mitochondria have a separate thioredoxin system. Plants have chloroplast thioredoxins, which via ferredoxin-thioredoxin reductase regulates photosynthetic enzymes by light. Thioredoxins are critical for redox regulation of protein function and signaling via thiol redox control. A growing number of transcription factors including NF-kappaB or the Ref-1-dependent AP1 require thioredoxin reduction for DNA binding. The cytosolic mammalian thioredoxin, lack of which is embryonically lethal, has numerous functions in defense against oxidative stress, control of growth and apoptosis, but is also secreted and has co-cytokine and chemokine activities. Thioredoxin reductase is a specific dimeric 70-kDa flavoprotein in bacteria, fungi and plants with a redox active site disulfide/dithiol. In contrast, thioredoxin reductases of higher eukaryotes are larger (112-130 kDa), selenium-dependent dimeric flavoproteins with a broad substrate specificity that also reduce nondisulfide substrates such as hydroperoxides, vitamin C or selenite. All mammalian thioredoxin reductase isozymes are homologous to glutathione reductase and contain a conserved C-terminal elongation with a cysteine-selenocysteine sequence forming a redox-active selenenylsulfide/selenolthiol active site and are inhibited by goldthioglucose (aurothioglucose) and other clinically used drugs. (85 Refs.)

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Thioredoxin--metabolism--ME; *Thioredoxin Reductase (NADPH)--metabolism--ME; Amino Acid Sequence; Animals; Base Sequence; Signal Transduction; Thioredoxin Reductase (NADPH)--chemistry--CH; Thioredoxin Reductase (NADPH)--genetics--GE

CAS Registry No.: 52500-60-4 (Thioredoxin)

Enzyme No.: EC 1.6.4.5 (Thioredoxin Reductase (NADPH))

Record Date Created: 20001128

Record Date Completed: 20001128

14/9/10

10569168 PMID: 10671551

The thioredoxin system of Helicobacter pylori.

Windle H J; Fox A; Ni Eidhin D; Kelleher D

Department of Clinical Medicine, Trinity College Dublin, Trinity Centre for Health Sciences, St. James's Hospital, Dublin 8, Ireland. wjwindle@tcd.ie

Journal of biological chemistry (UNITED STATES) Feb 18 2000, 275 (7) p5081-9, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed
Subfile: INDEX MEDICUS

This paper describes the purification of thioredoxin reductase (TR) and the characterization, purification, and cloning of thioredoxin (Trx) from Helicobacter pylori. Purification, amino acid sequence analysis, and molecular cloning of the gene encoding thioredoxin revealed that it is a 12-kDa protein which possesses the conserved redox active motif **CGPC** . The gene encoding Trx was amplified by polymerase chain reaction and inserted into a pET expression vector and used to transform Escherichia coli. Trx was overexpressed by induction with isopropyl-1-thio-beta-D-galactopyranosi de as a decahistidine fusion protein and was recovered from the cytoplasm as a soluble and active protein. The redox activity of this protein was characterized using several mammalian proteins of different architecture but all containing disulfide bonds. H. pylori thioredoxin efficiently reduced insulin, human immunoglobulins (IgG/IgA/sIgA), and soluble mucin. Subcellular fractionation analysis of H. pylori revealed that thioredoxin was associated largely with the cytoplasm and inner membrane fractions of the cell in addition to being recovered in the phosphate-buffered saline-soluble fraction of freshly harvested cells. H. pylori TR was purified to homogeneity by chromatography on DEAE-52, Cibacron blue 3GA, and 2',5'-ADP-agarose. Gel filtration revealed that the native TR had a molecular mass of 70 kDa which represented a homodimer composed of two 35-kDa subunits, as determined by SDS-polyacrylamide gel electrophoresis. H. pylori TR (NADPH-dependent) efficiently catalyzed the reduction of 5,5'-dithiobis(nitrobenzoic acid) in the presence of either native or recombinant H. pylori Trx. H. pylori Trx behaved also as a stress response element as broth grown bacteria secreted Trx in response to chemical, biological, and environmental stresses. These observations suggest that Trx may conceivably assist H. pylori in the process of colonization by inducing focal disruption of the oligomeric structure of mucin while rendering host antibody inactive through catalytic reduction.

Tags: Human

Descriptors: *Helicobacter pylori--genetics--GE; *Thioredoxin--genetics --GE; Amino Acid Sequence; Base Sequence; Cloning, Molecular; DNA Primers; Electrophoresis, Gel, Two-Dimensional; Escherichia coli--genetics--GE; Helicobacter pylori--enzymology--EN; Helicobacter pylori--metabolism--ME; Immunoglobulin A--metabolism--ME; Insulin--metabolism--ME; Molecular Sequence Data; Mucins--metabolism--ME; Sequence Homology, Amino Acid; Subcellular Fractions--metabolism--ME; Thioredoxin --isolation and purification--IP; Thioredoxin--metabolism--ME; Thioredoxin Reductase (NADPH)--isolation and purification--IP; Thioredoxin Reductase (NADPH) --metabolism--ME

Molecular Sequence Databank No.: GENBANK/AE000594

CAS Registry No.: 0 (DNA Primers); 0 (Immunoglobulin A); 0 (Mucins) ; 11061-68-0 (Insulin); 52500-60-4 (Thioredoxin)

Enzyme No.: EC 1.6.4.5 (Thioredoxin Reductase (NADPH))

Record Date Created: 20000321

Record Date Completed: 20000321

14/9/11

DIALOG(R)File 155:MEDLINE(R)

09682670 PMID: 8477381

Academic family medicine in Canada.

Hennen B K

Department of Family Medicine, University of Western Ontario, London.

CMAJ - Canadian Medical Association journal = journal de l'Association medicale canadienne (CANADA) May 1 1993, 148 (9) p1559-63, ISSN 0820-3946 Journal Code: 9711805

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Fifty years ago family practice in Canada had no academic presence.

13/9/23
DIALOG(R)File 155:MEDLINE(R)

11188177 PMID: 11232604

Thioredoxin **inhibits tumor necrosis factor- or interleukin-1-induced NF-kappaB activation at a level upstream of NF-kappaB-inducing kinase.**

Takeuchi J; Hirota K; Itoh T; Shinkura R; Kitada K; Yodoi J; Namba T; Fukuda K

Department of Anesthesia, Kyoto University Hospital, Japan.

Antioxidants & redox signalling (United States) Spring 2000, 2 (1) p83-92, ISSN 1523-0864 Journal Code: 100888899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Gene induction by tumor necrosis factor-alpha (TNFalpha) or interleukin-1beta (IL-1beta) is mediated in part by activation of the transcription factor nuclear factor kappaB (NF-kappaB), and requires signal adaptor molecules such as TNF receptor-associated factor (TRAFs). The latter interact with the NF-kappaB-inducing kinase (NIK), which is believed to be part of the IkappaB kinase complex. Although the precise mechanism is to be elucidated, it is well-known that antioxidant treatments inhibit the inflammatory cytokine-induced NF-kappaB activation. **Thioredoxin** (TRX) is a 12-kDa endogenous protein that regulates various cellular functions by modulating the redox state of proteins, overexpression of this molecule inhibits NF-kappaB activation. To elucidate the roles of TRX in the signal transduction of the cytokines, we investigated the effects of TRX on NF-kappaB activation induced by cytokine treatment or by overexpression of the signaling molecules. Our data show that TRX treatment inhibits NF-kappaB-dependent transcription at the level of downstream of TRAFs and upstream of NIK: TRX inhibited TRAF2-, TRAF5-, and TRAF6-induced NF-kappaB activation but does not inhibit NIK-, IKKalpha-, and MEKK-induced activation. In addition, we show that TRX inhibits NF-kappaB activation in a manner different from that for SAPK (stress activated protein kinase) inhibition.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Interleukin-1--antagonists and inhibitors--AI; * **NF-kappa B** --metabolism--ME; *Signal Transduction--drug effects--DE; * **Thioredoxin** --pharmacology--PD; *Transcription, Genetic--drug effects--DE; *Tumor Necrosis Factor--antagonists and inhibitors--AI; Acetylcysteine --pharmacology--PD; Antioxidants--pharmacology--PD; Carrier Proteins --physiology--PH; Cell Line--drug effects--DE; Genes, Reporter; Hela Cells --drug effects--DE; Interleukin-1--pharmacology--PD; Kidney; Luciferase --analysis--AN; Luciferase--genetics--GE; MAP Kinase Kinase Kinases --metabolism--ME; Mitogen-Activated Protein Kinases --antagonists and inhibitors--AI; Mutagenesis, Site-Directed; Oxidation-Reduction; Phosphorylation--drug effects--DE; Protein Processing, Post-Translational --drug effects--DE; Protein-Serine-Threonine Kinases--metabolism--ME; Proteins--antagonists and inhibitors--AI; Recombinant Proteins--antagonists and inhibitors--AI; Recombinant Proteins--pharmacology--PD; **Thioredoxin** --genetics--GE; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (Antioxidants); 0 (Carrier Proteins); 0 (Interleukin-1); 0 (NF-kappa B); 0 (Proteins); 0 (Recombinant Proteins); 0 (TNF receptor-associated factor 2); 0 (TNF receptor-associated factor 5); 0 (TNF receptor-associated factor 6); 0 (TRAF and TNF receptor-associated protein); 0 (Tumor Necrosis Factor); 52500-60-4 (Thioredoxin); 616-91-1 (Acetylcysteine)

Enzyme No.: EC 1.13.12.- (Luciferase); EC 2.7.1.- (I kappa B kinase); EC 2.7.1.37 (MAP Kinase Kinase Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Protein-Serine-Threonine Kinases); EC 2.7.10.- (MAPK kinase kinase 5); EC 2.7.10.- (mitogen-activated protein kinase p38)

Record Date Created: 20010305

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Geranylgeranylacetone (GGA) has been introduced into the clinical field as an anti-ulcer drug. In addition to protective effects on gastric mucosal cells, GGA also has anti-apoptotic effects against ischemia and reperfusion injury in hepatocytes and intestinal cells. However, the molecular mechanisms of the cytoprotective or anti-apoptotic effect of GGA are largely unknown. To explore the molecular mechanism of GGA action, we focused on **thioredoxin** (TRX), an endogenous-redox-acting molecule. We have demonstrated that GGA induces the messenger RNA and protein of TRX and affects the activation of transcription factors, AP-1 and NF-kappaB, and that GGA blunted ethanol-induced cytotoxicity of cultured hepatocytes. These results provide evidence suggesting that a possible novel molecular mechanism of GGA is to protect cells via the induction of TRX and the activation of transcription factors such as NF-kappaB and AP-1. Copyright 2000 Academic Press.

Tags: Human; Male; Support, Non-U.S. Gov't

Descriptors: Anti-Ulcer Agents--pharmacology--PD; *Apoptosis --drug effects--DE; *Diterpenes--pharmacology--PD; *Ethanol --antagonists and inhibitors--AI; *Liver--drug effects--DE; * **Thioredoxin** --metabolism--ME; Animals; Cell Line; Cells, Cultured; Ethanol--toxicity--TO; Gene Expression Regulation--drug effects--DE; Genes, Reporter; Liver--cytology--CY; Liver --metabolism--ME; **NF-kappa B** --metabolism--ME; RNA, Messenger--genetics --GE; RNA, Messenger--metabolism--ME; Rats; Rats, Wistar; Reverse Transcriptase Polymerase Chain Reaction; Tetradecanoylphorbol Acetate --pharmacology--PD; **Thioredoxin** --genetics--GE; Transcription Factor AP-1 --metabolism--ME; Transfection; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (Anti-Ulcer Agents); 0 (Diterpenes); 0 (NF-kappa B); 0 (RNA, Messenger); 0 (Transcription Factor AP-1); 0 (Tumor Necrosis Factor); 16561-29-8 (Tetradecanoylphorbol Acetate); 52500-60-4 (Thioredoxin); 64-17-5 (Ethanol); 6809-52-5 (geranylgeranylacetone)

Record Date Created: 20001019
Record Date Completed: 20001019

13/9/28

DIALOG(R)File 155:MEDLINE(R)

10784520 PMID: 10903915

Nucleoredoxin, glutaredoxin, and thioredoxin **differentially regulate NF-kappaB, AP-1, and CREB activation in HEK293 cells.**

Hirota K; Matsui M; Murata M; Takashima Y; Cheng F S; Itoh T; Fukuda K; Yodoi J

Department of Anesthesia, Kyoto University Hospital, Kyoto University, 54 Shogoin-Kawaharacho, Sakyo-Ku, Kyoto, 606-8507, Japan. khirota@kuhp.kyoto-u.ac.jp

Biochemical and biophysical research communications (UNITED STATES) Jul 21 2000, 274 (1) p177-82, ISSN 0006-291X Journal Code: 0372516

Erratum in Biochem Biophys Res Commun 2000 Aug 18;275(1) 247; Erratum in Note Junji Y [corrected to Yodoi J]

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Well-established mechanisms for regulation of protein activity include thiol-mediated oxidoreduction in addition to protein-protein interactions and phosphorylation. Nucleoredoxin (NRX), glutaredoxin (GRX), and **thioredoxin** (TRX) have been shown to act as a potent thiol reductase and reactive oxygen species regulator. They constitute a oxidoreductase superfamily and have been suggested as a candidate operating in the redox regulation of gene expression. We demonstrated here that intracellular localization of these redox molecules differ from each other and that the

redox molecules differentially regulate NF-kappaB, AP-1, and CREB activation induced by TNFalpha, PMA, and forskolin and by expression of signaling intermediate kinases, NIK, MEKK, and PKA in HEK293 cells. This is a first report that describes involvement of NRX and GRX and differences from TRX in transcriptional regulation of NF-kappaB, AP-1, and CREB in living cells. Copyright 2000 Academic Press.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: DNA-Binding Protein, Cyclic AMP-Responsive--metabolism--ME; *Gene Expression Regulation; * **NF-kappa B** --metabolism--ME; *Nuclear Proteins--metabolism--ME; *Oxidoreductases--metabolism--ME; *Proteins --metabolism--ME; *Saccharomyces cerevisiae Proteins; * **Thioredoxin** --metabolism--ME; *Transcription Factor AP-1--metabolism--ME; *Transcription, Genetic; 3T3 Cells; Animals; Blotting, Western; Cell Line; Cyclic AMP-Dependent Protein Kinases--metabolism--ME; Fluorescent Antibody Technique, Indirect; Forskolin--pharmacology--PD; Fungal Proteins --metabolism--ME; Mice; Oxidation-Reduction; Plasmids--metabolism--ME; Protein-Serine-Threonine Kinases--metabolism--ME; Signal Transduction; Tetradecanoylphorbol Acetate--pharmacology--PD; Transcription Factors --metabolism--ME; Transfection; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (DNA-Binding Protein, Cyclic AMP-Responsive); 0 (Fungal Proteins); 0 (GAL4 protein, S cerevisiae); 0 (NF-kappa B); 0 (Nuclear Proteins); 0 (Plasmids); 0 (Proteins); 0 (Saccharomyces cerevisiae Proteins); 0 (Transcription Factor AP-1); 0 (Transcription Factors); 0 (Tumor Necrosis Factor); 0 (glutaredoxin); 0 (nucleoredoxin); 16561-29-8 (Tetradecanoylphorbol Acetate); 52500-60-4 (Thioredoxin); 66428-89-5 (Forskolin)

Enzyme No.: EC 1. (Oxidoreductases); EC 2.7.1.- (MEK kinase); EC 2.7.1.37 (Cyclic AMP-Dependent Protein Kinases); EC 2.7.1.37 (Protein-Serine-Threonine Kinases)

Record Date Created: 20000831

Record Date Completed: 20000831

13/9/29

DIALOG(R)File 155:MEDLINE(R)

10688719 PMID: 10802230

Reactive oxygen species and proinflammatory cytokine signaling in endothelial cells: effect of selenium supplementation.

Tolando R; Jovanovic A; Brigelius-Flohe R; Ursini F; Maiorino M

Dipartimento di Chimica Biologica, Padova, Italy.

Free radical biology & medicine (UNITED STATES) Mar 15 2000, 28 (6) p979-86, ISSN 0891-5849 Journal Code: 8709159

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The release of superoxide (O(2)(*-)) and hydrogen peroxide (H(2)O(2)), induced by tumor necrosis factor-alpha (TNF-alpha) or interleukin-1beta (IL-1beta), has been studied in the endothelial cell line ECV 304 in the presence and absence of selenium (Se) supplementation. Both cytokines elicit the production of both species. Selenium supplementation, which increases Se-enzyme activity, decreases the amount of H(2)O(2) but not O(2)(*-) detectable in the extracellular medium. Inhibition of reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase by diphenyliodonium (DPI) or phenylarsine oxide (PAO), largely prevents O(2)(*-) production, whereas H(2)O(2) remains above the amount accounted for by disproportion of residual O(2)(*-). Thus, a fraction of H(2)O(2) found in the medium, derives from an intracellular pool, which is under control of selenium-dependent peroxidases. This is further supported by the observation that in Se-supplemented cells, the rate of intracellular glutathione (GSH) depletion induced by cytokine treatment is faster and more extensive. Because Se supplementation decreases cytokine-induced NF-kappaB activity, whereas added H(2)O(2) is inactive and catalase does not affect the activation induced by TNF-alpha, it is concluded that only

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              54  S11
              11  S12
     S13      43  S11 NOT S12
?t s13/9/all
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13/9/1

DIALOG(R)File 155:MEDLINE(R)

14519363 PMID: 10516220

Nitric oxide-induced reduction of lung cell and whole lung thioredoxin **expression is regulated by NF-kappaB.**

Zhang J; Velsor L W; Patel J M; Postlethwait E M; Block E R
Department of Medicine, University of Florida, 32068, USA.

American journal of physiology (UNITED STATES) Oct 1999, 277 (4 Pt 1) pL787-93, ISSN 0002-9513 Journal Code: 0370511
Contract/Grant No.: HL-54679; HL; NHLBI; HL-58679; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

We examined whether nitric oxide (NO)-induced inhibition of **thioredoxin** (Thx) expression is regulated by a mechanism mediated by a transcription factor, i.e., nuclear factor-kappaB (NF-kappaB), in cultured porcine pulmonary artery endothelial cells (PAEC) and in mouse lungs. Western blot analysis revealed that IkappaB-alpha content was reduced by 20 and 60% in PAEC exposed to 8.5 ppm NO for 2 and 24 h, respectively. NO exposure also caused significant reductions of cytosol fraction p65 and p52 content in PAEC. The nuclear fraction p65 and p52 contents were significantly reduced only in PAEC exposed to NO for 24 h. Exposure to NO resulted in a 50% reduction of p52 mRNA but not of the IkappaB-alpha subunit. DNA binding activity of the oligonucleotide encoding the NF-kappaB sequence in the Thx gene was significantly reduced in PAEC exposed to NO for 24 h. Exposure of mice to 10 ppm NO for 24 h resulted in a significant reduction of lung Thx and IkappaB-alpha mRNA and protein expression and in the oligonucleotide encoding Thx and NF-kappaB/DNA binding. These results 1) demonstrate that the effects of NO exposure on Thx expression in PAEC are comparable to those observed in intact lung and 2) suggest that reduced expression of the NF-kappaB subunit, leading to reduced NF-kappaB/DNA binding, is associated with the loss of Thx expression in PAEC and in intact mouse lungs.

Tags: Male; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: Lung--metabolism--ME; * **NF-kappa B** --physiology--PH; *Nitric Oxide--physiology--PH; * **Thioredoxin** --metabolism--ME; Animals; Cells, Cultured; DNA--metabolism--ME; Endothelium, Vascular--cytology--CY; Endothelium, Vascular--metabolism--ME; Gene Expression--physiology--PH; **I-kappa B** --genetics--GE; **I-kappa B** --metabolism--ME; Lung--cytology--CY ; Lung--enzymology--EN; Mice; Mice, Inbred C57BL; **NF-kappa B** --genetics --GE; **NF-kappa B** --metabolism--ME; Nitric Oxide--pharmacology--PD; Nitric-Oxide Synthase--metabolism--ME; Pulmonary Artery--cytology--CY; Pulmonary Artery--metabolism--ME; RNA, Messenger--metabolism--ME; Swine; **Thioredoxin** --genetics--GE
CAS Registry No.: 0 (I-kappa B); 0 (NF-kappa B); 0 (NF-kappa B p50) ; 0 (NF-kappa B p65); 0 (RNA, Messenger); 10102-43-9 (Nitric Oxide); 52500-60-4 (Thioredoxin); 9007-49-2 (DNA)
Enzyme No.: EC 1.14.13.39 (Nitric-Oxide Synthase)
Record Date Created: 19991122
Record Date Completed: 19991122

13/9/2

DIALOG(R)File 155:MEDLINE(R)

14491962 PMID: 10488136

Distinct roles of thioredoxin **in the cytoplasm and in the nucleus. A two-step mechanism of redox regulation of transcription factor NF-kappaB.**

Hirota K; Murata M; Sachi Y; Nakamura H; Takeuchi J; Mori K; Yodoi J
Department of Anesthesia, Kyoto University Hospital, Institute for Virus Research, Kyoto University, 53 Shogoin-Kawaharacho, Sakyo-Ku, Kyoto, 606-01, Japan.
Journal of biological chemistry (UNITED STATES) Sep 24 1999, 274 (39) p27891-7, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Oxidative stresses such as UV irradiation to mammalian cells triggers a variety of oxistress responses including activation of transcription factors. Recently, activation of nuclear factor-kappaB (NF-kappaB) has been shown to be under oxidoreduction (redox) regulation controlled by **thioredoxin** (TRX), which is one of major endogenous redox-regulating molecules with thiol reducing activity. In order to elucidate where in the cellular compartment TRX participates in NF-kappaB regulation, we investigated the intracellular localization of TRX. UVB irradiation induced translocation of TRX from the cytoplasm into the nucleus. In our in vitro diamide-induced cross-linking study, we showed that TRX can associate directly with NF-kappaB p50. Overexpression of wild-type TRX suppressed induction of luciferase activity under NF-kappaB-binding sites in response to UV irradiation compared with the mock transfectant. In contrast, overexpression of nuclear-targeted TRX enhanced the luciferase activity. Thus, TRX seems to play dual and opposing roles in the regulation of NF-kappaB. In the cytoplasm, it interferes with the signals to IkappaB kinases and blocks the degradation of IkappaB. In the nucleus, however, TRX enhances NF-kappaB transcriptional activities by enhancing its ability to bind DNA. This two-step TRX-dependent regulation of the NF-kappaB complex may be a novel activation mechanism of redox-sensitive transcription factors.

Tags: Human; Support, Non-U.S. Gov't
Descriptors: Cell Nucleus--metabolism--ME; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --metabolism--ME; Cell Line, Transformed; Cell Nucleus--drug effects--DE; Cytoplasm--drug effects--DE; Cytoplasm--metabolism--ME; Genes, Reporter; Hela Cells; Keratinocytes--cytology--CY; Keratinocytes --metabolism--ME; Keratinocytes--radiation effects--RE; Luciferase --genetics--GE; Microscopy, Confocal; **NF-kappa B** --radiation effects--RE; Oxidation-Reduction; Tetradecanoylphorbol Acetate--pharmacology--PD; Transfection; Tumor Cells, Cultured; Tumor Necrosis Factor--pharmacology --PD; Ultraviolet Rays
CAS Registry No.: 0 (NF-kappa B); 0 (Tumor Necrosis Factor); 16561-29-8 (Tetradecanoylphorbol Acetate); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 1.13.12.- (Luciferase)
Record Date Created: 19991104
Record Date Completed: 19991104

13/9/3
DIALOG(R)File 155:MEDLINE(R)

14465039 PMID: 10463612
Nuclear factor kappaB transactivation is increased but is not involved in the proliferative effects of thioredoxin **overexpression in MCF-7 breast cancer cells.**
Freemerman A J; Gallegos A; Powis G
Arizona Cancer Center, University of Arizona, Tucson 85724-5024, USA.
Cancer research (UNITED STATES) Aug 15 1999, 59 (16) p4090-4, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: CA48725; CA; NCI; CA77204; CA; NCI; F32CA76774; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

transcriptional regulator for production of IL-6 and IL-8 on stimulation with TNF-alpha. Consistent with these findings, the IkappaBalpha phosphorylation at Ser32 and its subsequent degradation in response to TNF-alpha was facilitated by TRX. These findings indicate that the elevated TRX concentration in SF of RA patients might be involved in the aggravation of rheumatoid inflammation by augmenting the NF-kappaB activation pathway.

Tags: Female; Human; Male; Support, Non-U.S. Gov't

Descriptors: Adjuvants, Immunologic--physiology--PH; *Arthritis, Rheumatoid--metabolism--ME; *Fibroblasts--immunology--IM; * **I-kappa B** ; *Interleukin-6--biosynthesis--BI; *Interleukin-8--biosynthesis--BI; *Synovial Fluid--immunology--IM; * **Thioredoxin** --pharmacology--PD; *Tumor Necrosis Factor--physiology--PH; Adjuvants, Immunologic--metabolism--ME; Adult; Aged ; Aged, 80 and over; Arthritis, Rheumatoid--immunology--IM; Biological Transport--drug effects--DE; Biological Transport--immunology--IM; C-Reactive Protein--metabolism--ME; Cell Nucleus--drug effects--DE; Cell Nucleus--metabolism--ME; Cells, Cultured; DNA-Binding Proteins--metabolism --ME; Middle Aged; **NF-kappa B** --antagonists and inhibitors--AI; Osteoarthritis--immunology--IM; Regression Analysis; Synovial Fluid --cytology--CY; Synovial Fluid--metabolism--ME; **Thioredoxin** --metabolism --ME; Tumor Necrosis Factor--metabolism--ME

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (DNA-Binding Proteins) ; 0 (I-kappa B); 0 (Interleukin-6); 0 (Interleukin-8); 0 (NF-kappa B); 0 (Tumor Necrosis Factor); 139874-52-5 (NF-kappaB inhibitor alpha); 52500-60-4 (Thioredoxin); 9007-41-4 (C-Reactive Protein)

Record Date Created: 19990715

Record Date Completed: 19990715

13/9/5

DIALOG(R)File 155:MEDLINE(R)

13946421 PMID: 9647199

TRANK, a novel cytokine that activates NF-kappa B and c-Jun N-terminal kinase.

Haridas V; Ni J; Meager A; Su J; Yu G L; Zhai Y; Kyaw H; Akama K T; Hu J; Van Eldik L J; Aggarwal B B

Department of Molecular Oncology, The University of Texas M.D. Anderson Cancer Center, Houston 77030, USA.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Jul 1 1998, 161 (1) p1-6, ISSN 0022-1767 Journal Code: 2985117R

Contract/Grant No.: AG 3939; AG; NIA

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

We searched the expressed sequence tag database using sequence homology and identified a novel cytokine, which we have named TRANK (**thioredoxin** peroxidase-related activator of NF-kappa B and c-Jun N-terminal kinase). The predicted amino acid sequence of TRANK was highly homologous to that of the thiol-specific antioxidant proteins. Unlike these proteins, however, TRANK had a putative secretory signal polypeptide and was found to be secreted by cells. TRANK was expressed in most tissues and cell lines, and the gene that encodes it was mapped to chromosome Xp21-22.1. TRANK activated NF-kappa B and induced the degradation of the inhibitory subunit of NF-kappa B. In addition, TRANK up-regulated the expression of NF-kappa B-dependent gene products, ICAM-1, and inducible nitric oxide synthase. TRANK also activated c-Jun N-terminal kinase and induced the proliferation of normal human foreskin fibroblasts. Its homology with antioxidant proteins, wide distribution in tissues, and ability to activate NF-kappa B and c-Jun N-terminal kinase suggest that TRANK plays an important role in inflammation.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: Ca(2+)-Calmodulin Dependent Protein Kinase--metabolism--ME; *Cytokines--physiology--PH; *Mitogen-Activated Protein Kinases; * **NF-kappa B** --metabolism--ME; Amino Acid Sequence; Antioxidants--pharmacology--PD;

Blood Proteins--chemistry--CH; Cell Division--drug effects--DE; Cell Line; Cytokines--biosynthesis--BI; Cytokines--genetics--GE; Cytokines--isolation and purification--IP; Enzyme Induction--drug effects--DE; Intercellular Adhesion Molecule-1--biosynthesis--BI; Molecular Sequence Data; Nitric-Oxide Synthase--biosynthesis--BI; Organ Specificity--genetics--GE; Sequence Homology, Amino Acid

CAS Registry No.: 0 (Antioxidants); 0 (Blood Proteins); 0 (Cytokines); 0 (NF-kappa B); 0 (TRANK protein); 0 (natural killer enhancing factor B); 126547-89-5 (Intercellular Adhesion Molecule-1)

Enzyme No.: EC 1.14.13.- (inducible nitric oxide synthase); EC 1.14.13.39 (Nitric-Oxide Synthase); EC 2.7.1.123 (Ca(2+)-Calmodulin Dependent Protein Kinase); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.10.- (c-Jun amino-terminal kinase)

Record Date Created: 19980709

Record Date Completed: 19980709

13/9/6

DIALOG(R)File 155:MEDLINE(R)

13807304 PMID: 9497357

Mammalian peroxiredoxin isoforms can reduce hydrogen peroxide generated in response to growth factors and tumor necrosis factor-alpha.

Kang S W; Chae H Z; Seo M S; Kim K; Baines I C; Rhee S G

Laboratory of Cell Signaling, NHLBI, National Institutes of Health, Bethesda, Maryland 20892, USA.

Journal of biological chemistry (UNITED STATES) Mar 13 1998, 273 (11) p6297-302, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Mammalian tissues express three immunologically distinct peroxiredoxin (Prx) proteins (Prx I, II, and III), which are the products of distinct genes. With the use of recombinant proteins Prx I, II, and III, all have now been shown to possess peroxidase activity and to rely on Trx as a source of reducing equivalents for the reduction of H2O2. Prx I and II are cytosolic proteins, whereas Prx III is localized in mitochondria. Transient overexpression of Prx I or II in cultured cells showed that they were able to eliminate the intracellular H2O2 generated in response to growth factors. Moreover, the activation of nuclear factor kappaB (NFkappaB) induced by extracellularly added H2O2 or tumor necrosis factor-alpha was blocked by overproduction of Prx II. These results suggest that, together with glutathione peroxidase and catalase, Prx enzymes likely play an important role in eliminating peroxides generated during metabolism. In addition, Prx I and II might participate in the signaling cascades of growth factors and tumor necrosis factor-alpha by regulating the intracellular concentration of H2O2.

Tags: Comparative Study; Human

Descriptors: Cytokines--pharmacology--PD; *Hydrogen Peroxide--metabolism--ME; *Isoenzymes--metabolism--ME; *Peroxidases--metabolism--ME; ***Thioredoxin*** --metabolism--ME; Animals; Glutathione Reductase--metabolism--ME; Growth Substances--pharmacology--PD; Hela Cells; Isoenzymes--genetics--GE; Mice; **NF-kappa B** --metabolism--ME; Oxidation-Reduction; Peroxidases--genetics--GE; Proteins; Rats; Recombinant Proteins--metabolism--ME; Signal Transduction; Species Specificity; Subcellular Fractions--enzymology--EN; **Thioredoxin** Reductase (NADPH)--metabolism--ME; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (Cytokines); 0 (Growth Substances); 0 (Isoenzymes); 0 (NF-kappa B); 0 (Proteins); 0 (Recombinant Proteins); 0 (Tumor Necrosis Factor); 52500-60-4 (Thioredoxin); 7722-84-1 (Hydrogen Peroxide)

Enzyme No.: EC 1.- (alkyl hydroperoxide reductase); EC 1.11.1. (Peroxidases); EC 1.11.1.- (protector protein (mixed-function oxidase systems)); EC 1.6.4.2 (Glutathione Reductase); EC 1.6.4.5 (**Thioredoxin**

Reductase (NADPH))
Record Date Created: 19980407
Record Date Completed: 19980407

13/9/7
DIALOG(R)File 155:MEDLINE(R)

13776193 PMID: 9475178
Overexpression of thioredoxin **in Fanconi anemia fibroblasts prevents the cytotoxic and DNA damaging effect of mitomycin C and diepoxybutane.**
Ruppitsch W; Meisslitzer C; Hirsch-Kauffmann M; Schweiger M
Institut fur Biochemie, Freie Universitat Berlin, Berlin-Dahlem, Germany. wrupp@chemie.fu-berlin.de
FEBS letters (NETHERLANDS) Jan 23 1998, 422 (1) p99-102, ISSN 0014-5793 Journal Code: 0155157
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Adult T cell leukemia derived factor (ADF)/ **thioredoxin** (Trx) is known to be an important intracellular antioxidant involved in a number of redox reactions such as ribonucleotide reductase (RNR) as well as of tyrosinase. Since RNR is a key enzyme of nucleotide metabolism and DNA synthesis, a reduced Trx level would result in reduced enzymatic activity and cause DNA damage. Furthermore, Trx is considered to be an effective regulator of redox sensitive gene expression. The role of Trx in nucleotide metabolism and gene expression may be an explanation for increased chromosomal instability as well as hypersensitivity towards oxygen, ROI and ROI generating agents. The activity of tyrosinase, the key enzyme of melanin biosynthesis, is influenced by the **thioredoxin** level and by superoxide radicals. Low **thioredoxin** levels and high superoxide concentrations activate tyrosinase causing hyperpigmentation of the skin. In addition to the observed high superoxide concentration in Fanconi anemia (FA) patients, a low **thioredoxin** level might be responsible for the hyperpigmentation (cafe-au-lait spots) in this disease. We observed that overexpression of the **thioredoxin** cDNA in FA fibroblasts completely abolished the DNA damaging effects of mitomycin C and diepoxybutane and inhibited the constitutive activity of the nuclear factor kappaB (NF-kappaB) in SV40 transformed FA fibroblasts. However, spontaneous chromosomal breakage was not affected.
Tags: Human; Male; Support, Non-U.S. Gov't
Descriptors: DNA Damage--drug effects--DE; *Epoxy Compounds--toxicity--TO ; *Fanconi Anemia--metabolism--ME; *Gene Expression Regulation--genetics --GE; *Mitomycin--toxicity--TO; * **Thioredoxin** --metabolism--ME; Antioxidants--metabolism--ME; Cell Line; Cell Survival--genetics--GE; Chromosome Breakage--genetics--GE; Cytokines--metabolism--ME; Epoxy Compounds--antagonists and inhibitors--AI; Micronucleus Tests; Mitomycin --antagonists and inhibitors--AI; **NF-kappa B** --metabolism--ME; Neoplasm Proteins--metabolism--ME; Oxidative Stress--physiology--PH; Transfection --genetics--GE; Transformation, Genetic--genetics--GE
CAS Registry No.: 0 (Antioxidants); 0 (Cytokines); 0 (Epoxy Compounds); 0 (NF-kappa B); 0 (Neoplasm Proteins); 0 (adult T cell leukemia-derived factor); 1464-53-5 (erythritol anhydride); 50-07-7 (Mitomycin); 52500-60-4 (Thioredoxin)
Record Date Created: 19980317
Record Date Completed: 19980317

13/9/8
DIALOG(R)File 155:MEDLINE(R)

13703533 PMID: 9371773
Inhibition of NF-kappaB DNA binding and nitric oxide induction in human T

cells and lung adenocarcinoma cells by selenite treatment.
Kim I Y; Stadtman T C
Laboratory of Biochemistry, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD 20892, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov 25 1997, 94 (24) p12904-7, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
NF-kappaB is a major transcription factor consisting of 50(p50)- and 65(p65)-kDa proteins that controls the expression of various genes, among which are those encoding cytokines, cell adhesion molecules, and inducible NO synthase (iNOS). After initial activation of NF-kappaB, which involves release and proteolysis of a bound inhibitor, essential cysteine residues are maintained in the active reduced state through the action of **thioredoxin** and **thioredoxin** reductase. In the present study, activation of NF-kappaB in human T cells and lung adenocarcinoma cells was induced by recombinant human tumor necrosis factor alpha or bacterial lipopolysaccharide. After lipopolysaccharide activation, nuclear extracts were treated with increasing concentrations of selenite, and the effects on DNA-binding activity of NF-kappaB were examined. Binding of NF-kappaB to nuclear responsive elements was decreased progressively by increasing selenite levels and, at 7 microM selenite, DNA-binding activity was completely inhibited. Selenite inhibition was reversed by addition of a dithiol, DTT. Proportional inhibition of iNOS activity as measured by decreased NO products in the medium (NO2- and NO3-) resulted from selenite addition to cell suspensions. This loss of iNOS activity was due to decreased synthesis of NO synthase protein. Selenium at low essential levels (nM) is required for synthesis of redox active selenoenzymes such as glutathione peroxidases and **thioredoxin** reductase, but in higher toxic levels (>5-10 microM) selenite can react with essential thiol groups on enzymes to form RS-Se-SR adducts with resultant inhibition of enzyme activity. Inhibition of NF-kappaB activity by selenite is presumed to be the result of adduct formation with the essential thiols of this transcription factor.
Tags: Human
Descriptors: Adenocarcinoma--metabolism--ME; *DNA--metabolism--ME; *Lung Neoplasms--metabolism--ME; * **NF-kappa B** --antagonists and inhibitors--AI; *Nitric Oxide--antagonists and inhibitors--AI; *Sodium Selenite --pharmacology--PD; *T-Lymphocytes--drug effects--DE; Adenocarcinoma --pathology--PA; Enzyme Induction; Jurkat Cells; Lung Neoplasms--pathology --PA; **NF-kappa B** --metabolism--ME; Nitric Oxide--biosynthesis--BI; Nitric-Oxide Synthase--biosynthesis--BI; Nitric-Oxide Synthase--genetics --GE; Protein Binding; T-Lymphocytes--metabolism--ME; Tumor Cells, Cultured
CAS Registry No.: 0 (NF-kappa B); 10102-18-8 (Sodium Selenite); 10102-43-9 (Nitric Oxide); 9007-49-2 (DNA)
Enzyme No.: EC 1.14.13.39 (Nitric-Oxide Synthase)
Record Date Created: 19980108
Record Date Completed: 19980108

13/9/9
DIALOG(R)File 155:MEDLINE(R)

13694568 PMID: 9388242
Regulatory role for a novel human thioredoxin **peroxidase in NF-kappaB activation.**
Jin D Y; Chae H Z; Rhee S G; Jeang K T
Laboratory of Molecular Microbiology, NIAID, National Institutes of Health, Bethesda, Maryland 20892, USA.
Journal of biological chemistry (UNITED STATES) Dec 5 1997, 272 (49) p30952-61, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

Reduction-oxidation (redox) plays a critical role in NF-kappaB activation. Diverse stimuli appear to utilize reactive oxygen species (e.g. hydrogen peroxide) as common effectors for activating NF-kappaB. Antioxidants govern intracellular redox status, and many such molecules can reduce H2O2. However, functionally, it does appear that different antioxidants are variously selective for redox regulation of certain transcription factors such as NF-kappaB. For NF-kappaB, **thioredoxin** has been described to be a more potent antioxidant than either glutathione or N-acetylcysteine. **Thioredoxin** peroxidase is the immediate enzyme that links reduction of H2O2 to **thioredoxin** . Several putative human **thioredoxin** peroxidases have been identified using recursive sequence searches/alignments with yeast or prokaryotic enzymes. None has been characterized in detail for intracellular function(s). Here, we describe a new human **thioredoxin** peroxidase, antioxidant enzyme AOE372, identified by virtue of its protein-protein interaction with the product of a proliferation association gene, pag, which is also a thiol-specific antioxidant. In human cells, AOE372 defines a redox pathway that specifically regulates NF-kappaB activity via a modulation of IkappaB-alpha phosphorylation in the cytoplasm. We show that AOE372 activity is regulated through either homo- or heterodimerization with other thiol peroxidases, implicating subunit assortment as a mechanism for regulating antioxidant specificities. AOE372 function suggests **thioredoxin** peroxidase as an immediate regulator of H2O2-mediated activation of NF-kappaB.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: **I-kappa B** ; * **NF-kappa B** --metabolism--ME; *Peroxidases; *Proteins--physiology--PH; Amino Acid Sequence; Antioxidants--metabolism --ME; Base Sequence; Cytoplasm--metabolism--ME; DNA-Binding Proteins --metabolism--ME; Dimerization; HIV Infections--enzymology--EN; HIV-1; Heat-Shock Proteins--metabolism--ME; Hela Cells; Molecular Sequence Data; Molecular Weight; Neoplasm Proteins--metabolism--ME; Oxidation-Reduction; Phosphorylation; Protein Binding; Proteins--chemistry--CH; Proteins --genetics--GE; RNA, Messenger--biosynthesis--BI; Tissue Distribution

Molecular Sequence Databank No.: GENBANK/U25182

CAS Registry No.: 0 (Antioxidants); 0 (DNA-Binding Proteins); 0 (Heat-Shock Proteins); 0 (I-kappa B); 0 (NF-kappa B); 0 (Neoplasm Proteins); 0 (Proteins); 0 (RNA, Messenger); 0 (antioxidant protein 1) ; 139874-52-5 (NF-kappaB inhibitor alpha)

Enzyme No.: EC 1.11.1. (Peroxidases); EC 1.11.1.- (Pag protein, human) ; EC 1.11.1.- (protector protein (mixed-function oxidase systems))

Record Date Created: 19980108
Record Date Completed: 19980108

13/9/10
DIALOG(R)File 155:MEDLINE(R)

13506317 PMID: 9192179

Regulation of NF-kappa B and disease control: identification of a novel serine kinase and thioredoxin **as effectors for signal transduction pathway for NF-kappa B activation.**

Okamoto T; Sakurada S; Yang J P; Merin J P

Department of Molecular Genetics, Nagoya City University Medical School, Japan.

Current topics in cellular regulation (UNITED STATES) 1997, 35 p149-61, ISSN 0070-2137 Journal Code: 2984740R

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

We have identified novel signal transduction cascades in activating NF-kappa B, as well as its pathogenetic roles in various disease processes.

By applying the basic knowledge obtained through these studies, we hope to find new therapeutic measures against currently incurable diseases such as hematogenic cancer cell metastasis, rheumatoid arthritis, and AIDS. We also propose a novel strategy in screening effective inhibitors against transcription factors. Elucidation of the cis-regulatory element for expression of pathogenetic genes and identification of the responsible transcription factor will not only facilitate the study of pathogenesis but will also promote the development of effective therapy. Recognition of control mechanisms of the NF-kappa B activation pathway has explained the therapeutic efficacy of various compounds with different pharmacologic actions. A similar strategy may be applicable for other inducible transcription factors. From the medical point of view, one of the purposes of these approaches is to find small molecular weight compounds that can be administered orally and that are effective in controlling gene expression of pathogenetic genes. (74 Refs.)

Tags: Human

Descriptors: **NF-kappa B** --metabolism--ME; Acquired Immunodeficiency Syndrome--etiology--ET; Acquired Immunodeficiency Syndrome--metabolism--ME ; Acquired Immunodeficiency Syndrome--virology--VI; Animals; Drug Evaluation, Preclinical; HIV--physiology--PH; **NF-kappa B** --antagonists and inhibitors--AI; Neoplasm Metastasis--physiopathology--PP; Oxidation-Reduction; Protein-Serine-Threonine Kinases--metabolism--ME; Reactive Oxygen Species--metabolism--ME; Signal Transduction; **Thioredoxin** --metabolism--ME ; Virus Replication

CAS Registry No.: 0 (NF-kappa B); 0 (Reactive Oxygen Species); 52500-60-4 (Thioredoxin)

Enzyme No.: EC 2.7.1.37 (Protein-Serine-Threonine Kinases)

Record Date Created: 19970813

Record Date Completed: 19970813

13/9/11

DIALOG(R)File 155:MEDLINE(R)

13410141 PMID: 9073573

Study of gene regulation by NF-kappa B and AP-1 in response to reactive oxygen intermediates.

Muller J M; Rupec R A; Baeuerle P A

Institute for Experimental Cancer Research, Tumor Biology Center, Freiburg, Germany.

Methods (San Diego, Calif.) (UNITED STATES) Mar 1997, 11 (3) p301-12 , ISSN 1046-2023 Journal Code: 9426302

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Reactive oxygen intermediates (ROIs), such as hydrogen peroxide or superoxide, are an evolutionarily ancient threat to all organisms. Exposure of bacteria to ROIs initiates a genetic program that coordinates the production of novel proteins with protective functions. This genetic response is mediated by regulatory proteins that have the potential to initiate transcription of genes when the levels of the ROIs increase. In plant cells, a variety of viral pathogens increase hydrogen peroxide production, which is required to mount a defensive genetic response. It was suggested that in this case H2O2 is used as a secondary messenger and an immediate-early pathogen signal. In higher vertebrates, two transcription factors, nuclear factor kappa B and activator protein 1, were found to respond to ROIs. Both are well studied: they are induced by a great variety of seemingly unrelated conditions and serve important roles in immune, inflammatory, and other pathogen-related genetic responses. In this article we discuss how the ROI responsiveness of transcription factors can be experimentally studied and summarize evidence to suggest that ROIs have been conserved during evolution as messengers of a general pathogen response. (90 Refs.)

Descriptors: Gene Expression Regulation; * **NF-kappa B** --metabolism--ME;

*Reactive Oxygen Species--metabolism--ME; *Transcription Factor AP-1 --metabolism--ME; Animals; Antioxidants--pharmacology--PD; Evolution, Molecular; Glutathione--metabolism--ME; Hydrogen Peroxide--pharmacology--PD ; Oxidation-Reduction; Proto-Oncogene Proteins--metabolism--ME; **Thioredoxin** --metabolism--ME

CAS Registry No.: 0 (Antioxidants); 0 (NF-kappa B); 0 (Proto-Oncogene Proteins); 0 (Reactive Oxygen Species); 0 (Transcription Factor AP-1); 0 (ets-domain protein elk-1); 52500-60-4 (Thioredoxin); 70-18-8 (Glutathione); 7722-84-1 (Hydrogen Peroxide)

Record Date Created: 19970425

Record Date Completed: 19970425

13/9/12

DIALOG(R)File 155:MEDLINE(R)

13360888 PMID: 9034250

Redox regulation of NF-kappa B activation.

Flohe L; Brigelius-Flohe R; Saliou C; Traber M G; Packer L

Department of Molecular and Cell Biology, University of California, Berkeley 94720-3200, USA.

Free radical biology & medicine (UNITED STATES) 1997, 22 (6) p1115-26, ISSN 0891-5849 Journal Code: 8709159

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Cytosolic reactions of the nuclear factor kappa B/inhibitor (NF-kappaB/IkappaB) complex leading to its activation, NF-kappaB translocation into the nucleus, DNA binding, and transactivation have been described with some degree of clarity, but the upstream processes that stimulate those cytosolic reactions remain obscure. These processes definitely involve multiple protein serine/threonine kinases, as proximal modifiers of IkappaB, as well as the corresponding phosphatases, upstream kinases, and phosphatases, including those acting on tyrosine residues. This complex cascade of phosphorylation and dephosphorylation is modulated by redox reactions of unknown nature in the sense that the oxidant status of the cytosol increases the phosphorylation and degradation of IkappaB. NF-kappaB action, however, requires a **thioredoxin** -dependent reduced status in the nucleus. Upstream kinase(s) and or phosphatase(s) prone to thiolation or oxidation of vicinal SH groups are at present considered the best candidates mediating the redox regulation of NF-kappaB. (117 Refs.)

Tags: Human

Descriptors: **NF-kappa B** --metabolism--ME; Animals; Antioxidants; Biological Transport; Cell Nucleus--metabolism--ME; Cytosol--metabolism--ME ; Hydrogen Peroxide--metabolism--ME; Oxidation-Reduction; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (Antioxidants); 0 (NF-kappa B); 0 (Tumor Necrosis Factor); 7722-84-1 (Hydrogen Peroxide)

Record Date Created: 19970826

Record Date Completed: 19970826

13/9/13

DIALOG(R)File 155:MEDLINE(R)

12970541 PMID: 8635688

Antioxidant and redox regulation of gene transcription.

Sen C K; Packer L

Department of Molecular and Cell Biology, University of California at Berkeley, California 94720-3200, USA.

FASEB journal - official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) May 1996, 10 (7) p709-20, ISSN 0892-6638 Journal Code: 8804484

Contract/Grant No.: CA 47597-07; CA; NCI; GM 27345-15; GM; NIGMS
Comment in FASEB J. 1997 Apr;11(5) 374-5; Comment in PMID 9141504
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

Reactive oxygen species (ROS) are implicated in the pathogenesis of a wide variety of human diseases. Recent evidence suggests that at moderately high concentrations, certain forms of ROS such as H202 may act as signal transduction messengers. To develop a better understanding of the exact mechanisms that underlie ROS-dependent disorders in biological systems, recent studies have investigated the regulation of gene expression by oxidants, antioxidants, and other determinants of the intracellular reduction-oxidation (redox) state. At least two well-defined transcription factors, nuclear factor (NF) kappa B and activator protein (AP) -1 have been identified to be regulated by the intracellular redox state. The regulation of gene expression by oxidants, antioxidants, and the redox state has emerged as a novel subdiscipline in molecular biology that has promising therapeutic implications. Binding sites of the redox-regulated transcription factors NF-kappa B and AP-1 are located in the promoter region of a large variety of genes that are directly involved in the pathogenesis of diseases, e.g., AIDS, cancer, atherosclerosis and diabetic complications. Biochemical and clinical studies have indicated that antioxidant therapy may be useful in the treatment of disease. Critical steps in the signal transduction cascade are sensitive to oxidants and antioxidants. Many basic events of cell regulation such as protein phosphorylation and binding of transcription factors to consensus sites on DNA are driven by physiological oxidant-antioxidant homeostasis, especially by the thiol-disulfide balance. Endogenous glutathione and **thioredoxin** systems, and the exogenous lipoate-dihydrolipoate couple may therefore be considered to be effective regulators of redox-sensitive gene expression. The efficacy of different antioxidants to favorably influence the molecular mechanisms implicated in human disease should be a critical determinant of its selection for clinical studies. (94 Refs.)

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: Antioxidants--metabolism--ME; * **NF-kappa B** --metabolism--ME; *Transcription Factor AP-1--metabolism--ME; *Transcription, Genetic; Animals; DNA--metabolism--ME; **NF-kappa B** --antagonists and inhibitors--AI; Oxidation-Reduction; Protein Binding; Reactive Oxygen Species--metabolism --ME

CAS Registry No.: 0 (Antioxidants); 0 (NF-kappa B); 0 (Reactive Oxygen Species); 0 (Transcription Factor AP-1); 9007-49-2 (DNA)

Record Date Created: 19960710
Record Date Completed: 19960710

13/9/14
DIALOG(R)File 155:MEDLINE(R)

12886752 PMID: 8555200

Ionization equilibria for side-chain carboxyl groups in oxidized and reduced human thioredoxin **and in the complex with its target peptide from the transcription factor NF kappa B.**

Qin J; Clore G M; Gronenborn A M

Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892-0520, USA.

Biochemistry (UNITED STATES) Jan 9 1996, 35 (1) p7-13, ISSN 0006-2960 Journal Code: 0370623

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The pH dependence of the 13C chemical shifts of the side-chain carboxyl

carbons of all Asp and Glu residues in the reduced and oxidized states of human **thioredoxin** and in a mixed disulfide complex of human **thioredoxin** with a target peptide from the transcription factor NF kappa B has been investigated by multidimensional triple-resonance NMR spectroscopy. While the titration curves for most of the side-chain carboxyl resonances exhibit simple Henderson-Hasselbalch behavior with pKa values not far from those found for model compounds, several side chains give rise to two- or three-step titration curves, indicative of the influence of multiple ionizations. In particular, the triad formed by Asp58, Asp60, and Asp61 forms such a complex network of titrating groups. The ionization behavior of Asp26 shows an abnormally high pKa value for an aspartate residue in all states of human **thioredoxin** , with pKa values of 9.9 in the reduced state, 8.1 in the oxidized state, 8.9 in the mixed disulfide complex, and 8.6 in an active site mutant in which Cys35 was replaced by Ala. The unambiguous determination of the pKa values of Asp26 for a variety of states of human **thioredoxin** presented in this paper is highly significant in view of two recent reports on Escherichia coli **thioredoxin** which presented contradicting pKa values for Asp26 and Cys35 [Wilson et al. (1995) Biochemistry 34, 8931-8939; Jeng et al. (1995) Biochemistry 34, 10101-10105]. The stabilization of the protonated side chain of Asp26 in human **thioredoxin** is achieved via a hydrogen-bonding network involving the hydroxyl group of the neighboring Ser28 which is then connected to the active site region (comprising Cys32 and Cys35) via bound water molecules. The coupling of the buried Asp26 to the active site is responsible for the influence of the Asp26 ionization behavior on the titration shifts of active site residues.

Tags: Comparative Study; Human; Support, U.S. Gov't, P.H.S.

Descriptors: **NF-kappa B** --chemistry--CH; * **NF-kappa B** --metabolism--ME; *Peptide Fragments--chemistry--CH; *Protein Conformation; * **Thioredoxin** --chemistry--CH; * **Thioredoxin** --metabolism--ME; Amino Acid Sequence; Carbon Isotopes; Cysteine; Hydrogen-Ion Concentration; Kinetics; Magnetic Resonance Spectroscopy--methods--MT; Models, Molecular; Mutagenesis, Site-Directed; Oxidation-Reduction; Peptide Fragments--metabolism--ME; Point Mutation; Recombinant Proteins--chemistry--CH; Recombinant Proteins --metabolism--ME

CAS Registry No.: 0 (Carbon Isotopes); 0 (NF-kappa B); 0 (Peptide Fragments); 0 (Recombinant Proteins); 52-90-4 (Cysteine); 52500-60-4 (Thioredoxin)

Record Date Created: 19960227

Record Date Completed: 19960227

13/9/15

DIALOG(R)File 155:MEDLINE(R)

12836136 PMID: 7476359

Effects of thioredoxin **on activation of transcription factor NF-kappa B.**

Schulze-Osthoff K; Schenk H; Droge W

Division of Immunochemistry, Deutsches Krebsforchungszentrum, Heidelberg, Germany.

Methods in enzymology (UNITED STATES) 1995, 252 p253-64, ISSN 0076-6879 Journal Code: 0212271

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Tags: Human

Descriptors: **NF-kappa B** --metabolism--ME; * **Thioredoxin** --pharmacology --PD; Base Sequence; Chloramphenicol O-Acetyltransferase--biosynthesis--BI; DNA Probes--metabolism--ME; Escherichia coli--genetics--GE; Gene Expression Regulation; Hela Cells; Molecular Sequence Data; **NF-kappa B** --drug effects --DE; Protein Binding; Protein Processing, Post-Translational; Recombinant Proteins--pharmacology--PD; **Thioredoxin** --genetics--GE; Trans-Activation (Genetics); Transfection

CAS Registry No.: 0 (DNA Probes); 0 (NF-kappa B); 0 (Recombinant Proteins); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase)
Record Date Created: 19951212
Record Date Completed: 19951212

13/9/16
DIALOG(R)File 155:MEDLINE(R)

12747598 PMID: 7545393
Inhibition of NF-kappa B by pyrrolidine dithiocarbamate blocks endothelial cell activation.
Ferran C; Millan M T; Csizmadia V; Cooper J T; Brostjan C; Bach F H; Winkler H
Sandoz Center for Immunobiology, New England Deaconess Hospital, Harvard Medical School, Boston, MA 02215, USA.
Biochemical and biophysical research communications (UNITED STATES) Sep 5 1995, 214 (1) p212-23, ISSN 0006-291X Journal Code: 0372516
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Endothelial cell activation is achieved by the rapid, protein synthesis-independent induction of a characteristic set of genes. Because of the abundance of binding sites for the transcription factor NF-kappa B in the regulatory region of the aforementioned genes, we hypothesized that this factor might play a key role. Reactive oxygen intermediates act as second messengers in the activation of NF-kappa B. We have used the antioxidant pyrrolidine dithiocarbamate to analyze the effect of NF-kappa B inhibition on TNF alpha-induced EC activation in vitro. We show that pyrrolidine dithiocarbamate strongly reduces the TNF alpha-mediated induction of E-selectin, VCAM-1, ICAM-1, PAI-1, tissue factor, IL-8 and I kappa B-alpha. We present evidence identifying NF-kappa B as a central of EC activation. Therefore, this factor may represent a prime target for therapeutic intervention in pathologic conditions associated with EC activation such as allo- and xenograft rejection, atherosclerosis, ischemic reperfusion injury and vasculitis.
Tags: Support, Non-U.S. Gov't
Descriptors: Antioxidants--pharmacology--PD; *Endothelium, Vascular--drug effects--DE; * **NF-kappa B** --antagonists and inhibitors--AI; *Pyrrolidines --pharmacology--PD; *Thiocarbamates--pharmacology--PD; Animals; Binding Sites; Cell Adhesion Molecules--genetics--GE; E-Selectin; Endothelium, Vascular--cytology--CY; Endothelium, Vascular--metabolism--ME; Gene Expression Regulation--drug effects--DE; Genes, jun; Glyceraldehyde-3-Phosphate Dehydrogenases--genetics--GE; Hydrogen Peroxide--metabolism--ME; **NF-kappa B** --metabolism--ME; RNA, Messenger--genetics--GE; RNA, Messenger --metabolism--ME; Regulatory Sequences, Nucleic Acid; Swine; **Thioredoxin** --genetics--GE
CAS Registry No.: 0 (Antioxidants); 0 (Cell Adhesion Molecules); 0 (E-Selectin); 0 (NF-kappa B); 0 (Pyrrolidines); 0 (RNA, Messenger); 0 (Thiocarbamates); 25769-03-3 (pyrrolidine dithiocarbamic acid); 52500-60-4 (Thioredoxin); 7722-84-1 (Hydrogen Peroxide)
Enzyme No.: EC 1.2.1.- (Glyceraldehyde-3-Phosphate Dehydrogenases)
Record Date Created: 19951012
Record Date Completed: 19951012

13/9/17
DIALOG(R)File 155:MEDLINE(R)

12663444 PMID: 7788295
Solution structure of human thioredoxin **in a mixed disulfide intermediate complex with its target peptide from the transcription factor**

NF kappa B.

Qin J; Clore G M; Kennedy W M; Huth J R; Gronenborn A M

Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892-0520, USA.

Structure (London, England) (ENGLAND) Mar 15 1995, 3 (3) p289-97, ISSN 0969-2126 Journal Code: 9418985

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

BACKGROUND: Human **thioredoxin** is a 12 kDa cellular redox protein that plays a key role in maintaining the redox environment of the cell. It has recently been shown to be responsible for activating the DNA-binding properties of the cellular transcription factor, NF kappa B, by reducing a disulfide bond involving Cys62 of the p50 subunit. Using multidimensional heteronuclear-edited and hetero-nuclear-filtered NMR spectroscopy, we have solved the solution structure of a complex of human **thioredoxin** and a 13-residue peptide extending from residues 56-68 of p50, representing a kinetically stable mixed disulfide intermediate along the reaction pathway. RESULTS: The NF kappa B peptide is located in a long boot-shaped cleft on the surface of human **thioredoxin** delineated by the active-site loop, helices alpha 2, alpha 3 and alpha 4, and strands beta 3 and beta 4. The peptide adopts a crescent-like conformation with a smooth 110 degrees bend centered around residue 60 which permits it to follow the path of the cleft. CONCLUSIONS: In addition to the intermolecular disulfide bridge between Cys32 of human **thioredoxin** and Cys62 of the peptide, the complex is stabilized by numerous hydrogen-bonding, electrostatic and hydrophobic interactions which involve residues 57-65 of the NF kappa B peptide and confer substrate specificity. These structural features permit one to suggest the specificity requirements for human **thioredoxin** -catalyzed disulfide bond reduction of proteins.

Tags: Human; Support, U.S. Gov't, P.H.S.

Descriptors: Disulfides--chemistry--CH; *Disulfides--metabolism--ME; * **NF-kappa B** --chemistry--CH; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --chemistry--CH; * **Thioredoxin** --metabolism--ME; Amino Acid Sequence; Magnetic Resonance Spectroscopy; Models, Molecular; Molecular Sequence Data ; Molecular Structure; Protein Conformation

CAS Registry No.: 0 (Disulfides); 0 (NF-kappa B); 52500-60-4 (Thioredoxin)

Record Date Created: 19950727

Record Date Completed: 19950727

13/9/18

DIALOG(R)File 155:MEDLINE(R)

11415408 PMID: 11410599

Nuclear factor kappa B is a molecular target for sulforaphane-mediated anti-inflammatory mechanisms.

Heiss E; Herhaus C; Klimo K; Bartsch H; Gerhauser C

Deutsches Krebsforschungszentrum Heidelberg, Division of Toxicology and Cancer Risk Factors, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany.

Journal of biological chemistry (United States) Aug 24 2001, 276 (34) p32008-15, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Sulforaphane (SFN), an aliphatic isothiocyanate, is a known cancer chemopreventive agent. Aiming to investigate anti-inflammatory mechanisms of SFN, we here report a potent decrease in lipopolysaccharide (LPS)-induced secretion of pro-inflammatory and pro-carcinogenic signaling factors in cultured Raw 264.7 macrophages after SFN treatment, i.e. NO,

prostaglandin E(2), and tumor necrosis factor alpha. SFN did not directly interact with NO, nor did it inhibit inducible nitric-oxide synthase enzymatic activity. Western blot analyses revealed time- and dose-dependent reduction of LPS-induced inducible nitric-oxide synthase as well as Cox-2 protein expression, which was suppressed at the transcriptional level. To reveal the target of SFN beyond its anti-inflammatory action, we performed electrophoretic mobility shift assay analyses of transcription factor-DNA binding. Consequently, nuclear factor kappa B (NF-kappa B), a pivotal transcription factor in LPS-stimulated pro-inflammatory response, was identified as the key mediator. SFN selectively reduced DNA binding of NF-kappa B without interfering with LPS-induced degradation of the inhibitor of NF-kappa B nor with nuclear translocation of NF-kappa B. Because SFN can interact with thiol groups by dithiocarbamate formation, it may impair the redox-sensitive DNA binding and transactivation of NF-kappa B. Sulforaphane could either directly inactivate NF-kappa B subunits by binding to essential Cys residues or interact with glutathione or other redox regulators like **thioredoxin** and Ref-1 relevant for NF-kappa B function. Our data provide novel evidence that anti-inflammatory mechanisms contribute to sulforaphane-mediated cancer chemoprevention.

Tags: Support, Non-U.S. Gov't

Descriptors: Anti-Inflammatory Agents, Non-Steroidal--pharmacology--PD; *Anticarcinogenic Agents--pharmacology--PD; * **NF-kappa B** --drug effects--DE; *Thiocyanates--pharmacology--PD; Animals; Cell Line; Cell Nucleus --metabolism--ME; DNA--metabolism--ME; Dinoprostone--biosynthesis--BI; Glutathione--metabolism--ME; Hydrolysis; **I-kappa B** --metabolism--ME; Isoenzymes--biosynthesis--BI; Isoenzymes--drug effects--DE; Isoenzymes --genetics--GE; Lipopolysaccharides--pharmacology--PD; Macrophages --drug effects--DE; Macrophages--metabolism--ME; Mice; **NF-kappa B** --metabolism --ME; Nitric Oxide--biosynthesis--BI; Nitric-Oxide Synthase--antagonists and inhibitors--AI; Nitric-Oxide Synthase--biosynthesis--BI; Nitric-Oxide Synthase--genetics--GE; Prostaglandin-Endoperoxide Synthase--biosynthesis --BI; Prostaglandin-Endoperoxide Synthase--drug effects--DE; Prostaglandin-Endoperoxide Synthase--genetics--GE; Protein Transport; RNA, Messenger--genetics--GE; RNA, Messenger--metabolism--ME; Reverse Transcriptase Polymerase Chain Reaction; Tumor Necrosis Factor --biosynthesis--BI; Tumor Necrosis Factor--drug effects--DE; Tumor Necrosis Factor--genetics--GE

CAS Registry No.: 0 (Anti-Inflammatory Agents, Non-Steroidal); 0 (Anticarcinogenic Agents); 0 (I-kappa B); 0 (Isoenzymes); 0 (Lipopolysaccharides); 0 (NF-kappa B); 0 (RNA, Messenger); 0 (Thiocyanates); 0 (Tumor Necrosis Factor); 10102-43-9 (Nitric Oxide); 363-24-6 (Dinoprostone); 4478-93-7 (sulforafan); 70-18-8 (Glutathione); 9007-49-2 (DNA)

Enzyme No.: EC 1.14.13.- (inducible nitric oxide synthase); EC 1.14.13.39 (Nitric-Oxide Synthase); EC 1.14.99.- (cyclooxygenase 2); EC 1.14.99.1 (Prostaglandin-Endoperoxide Synthase)

Record Date Created: 20010820

Record Date Completed: 20010920

Date of Electronic Publication: 20010615

13/9/19

DIALOG(R)File 155:MEDLINE(R)

11412818 PMID: 11509327

Activation of nuclear factor-kappa b transcriptional activity in airway epithelial cells by thioredoxin **but not by N-acetyl-cysteine and glutathione.**

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American journal of respiratory cell and molecular biology (United States) Aug 2001, 25 (2) p178-85, ISSN 1044-1549 Journal Code: 8917225

Contract/Grant No.: ES06230; ES; NIEHS; ES09703; ES; NIEHS; HL35635; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Increasing evidence indicates that intracellular redox status modulates the activity of various transcriptional factors, including nuclear factor (NF)-kappa B and activator protein-1. Our laboratory has been interested in characterizing the role **thioredoxin** (TRX) plays in regulating cellular redox status in airway epithelium. TRX is a small, ubiquitous protein with two redox-active half-cysteine residues, -Cys-Gly-Pro-Cys, in its active center. Using primary passage-1 human tracheobronchial epithelial cell cultures and an immortalized human bronchial epithelial cell line, HBE1, we observed that tumor necrosis factor (TNF)-alpha enhanced NF-kappa B transcriptional activity. This observation was based on gel mobility shift assays and interleukin (IL)-8 promoter-reporter gene transfection studies. TNF-alpha activation coincided with translocation of NF-kappa B p65 from the cytoplasm to the nucleus. Pretreatment with N-acetyl-cysteine (NAC) (1 to 10 mM) or glutathione (1 to 10 mM) inhibited TNF-alpha-induced activation of NF-kappa B transcriptional activity and IL-8 promoter-mediated reporter gene expression. In contrast, elevated TRX protein levels in cells enhanced TNF-alpha-dependent NF-kappa B transcriptional activity and IL-8 promoter activity. This observation was independent of the manner in which TRX was elevated in cells (e.g., by cotransfection with a FLAG-TRX expression clone, or by direct exposure to commercially available human TRX protein). Localization of TRX protein by anti-TRX antibody indicated an accumulation of TRX protein in the nucleus after TNF-alpha treatment. The nuclear localization phenomenon was different from the major cytosolic accumulation of glutathione and NAC. This is the first known report demonstrating movement of TRX into the nucleus of airway epithelial cells after an inflammatory stress. These results suggest a compartment effect of thiol chemicals in the regulation of redox-dependent transcriptional activity.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: Acetylcysteine--pharmacology--PD; *Bronchi--drug effects--DE; *Bronchi--metabolism--ME; *Glutathione--pharmacology--PD; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --pharmacology--PD; Cell Line; Cell Nucleus --drug effects--DE; Cell Nucleus--metabolism--ME; Cells, Cultured; DNA --genetics--GE; DNA--metabolism--ME; Epithelial Cells--drug effects--DE; Epithelial Cells--metabolism--ME; Gene Expression--drug effects--DE; Interleukin-8--genetics--GE; Oxidation-Reduction; **Thioredoxin** --metabolism --ME; Trachea--drug effects--DE; Trachea--metabolism--ME; Transcription, Genetic--drug effects--DE; Tumor Necrosis Factor--pharmacology--PD

CAS Registry No.: 0 (Interleukin-8); 0 (NF-kappa B); 0 (Tumor Necrosis Factor); 52500-60-4 (Thioredoxin); 616-91-1 (Acetylcysteine); 70-18-8 (Glutathione); 9007-49-2 (DNA)

Record Date Created: 20010817
Record Date Completed: 20011011

13/9/20
DIALOG(R)File 155:MEDLINE(R)

11353156 PMID: 11337489

Redox-sensitive transactivation of epidermal growth factor receptor by tumor necrosis factor confers the NF-kappa B activation.

Hirota K; Murata M; Itoh T; Yodoi J; Fukuda K

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Journal of biological chemistry (United States) Jul 13 2001, 276 (28) p25953-8, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Cross-communication between different signaling systems allows the integration of the great diversity of stimuli that a cell receives under varying physiological situations. In this paper we have explored the possibility that tumor necrosis factor (TNF) receptor signal cross-talks with epidermal growth factor (EGF) receptor signal on the nuclear factor-kappa B (NF-kappa B) activation pathway. We have demonstrated that overexpression of the EGF receptor (EGFR) in NIH3T3 cells significantly enhances TNF-induced NF-kappa B-dependent luciferase activity even without EGF, that EGF treatment has a synergistic effect on the induction of the reporter activity, and that this enhancement is suppressed by AG1478, EGFR-specific tyrosine kinase inhibitor. We also have shown that TNF induces tyrosine phosphorylation and internalization of the overexpressed EGFR in NIH3T3 cells and the endogenously expressed EGFR in A431 cells and that the transactivation by TNF is suppressed by N-acetyl-l-cysteine or overexpression of an endogenous reducing molecule, **thioredoxin** , but not by phosphatidylinositol 3-kinase inhibitors and protein kinase C inhibitor. Taken together, this evidence strongly suggests that EGFR transactivation by TNF, which is regulated in a redox-dependent manner, is playing a pivotal role in TNF-induced NF-kappa B activation.

Tags: Support, Non-U.S. Gov't

Descriptors: **NF-kappa B** --physiology--PH; *Receptor, Epidermal Growth Factor--physiology--PH; *Receptors, Tumor Necrosis Factor--physiology--PH; Animals; Cell Line; Fibroblasts; Mice; Oxidation-Reduction; Receptor Cross-Talk; Signal Transduction--genetics--GE; Trans-Activation (Genetics); Tumor Necrosis Factor--physiology--PH

CAS Registry No.: 0 (NF-kappa B); 0 (Receptors, Tumor Necrosis Factor) ; 0 (Tumor Necrosis Factor)

Enzyme No.: EC 2.7.1.112 (Receptor, Epidermal Growth Factor)

Record Date Created: 20010709

Record Date Completed: 20010816

Date of Electronic Publication: 20010503

13/9/21

DIALOG(R)File 155:MEDLINE(R)

11286477 PMID: 11063742

c-Jun NH2-terminal kinase-mediated redox-dependent degradation of IkappaB: role of thioredoxin **in NF-kappaB activation.**

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Journal of biological chemistry (United States) Feb 16 2001, 276 (7) p4662-70, ISSN 0021-9258 Journal Code: 2985121R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

NF-kappaB is a redox-sensitive transcription factor known to be activated by oxidative stress as well as chemical and biological reductants. Its DNA binding activity requires reduced cysteines present in the p65 subunit of the dimer. **Thioredoxin** (Trx) is an endogenous disulfide oxidoreductase known to modulate several redox-dependent functions in the cell. NF-kappaB was activated by addition of Escherichia coli **thioredoxin** in a redox-dependent manner in A549 cells. Such activation was accompanied by degradation of IkappaB in the cytosol. In addition, only the reduced form of **thioredoxin** activated NF-kappaB, whereas the oxidized form was without any effect. Overexpression of human **thioredoxin** also caused activation of NF-kappaB and degradation of IkappaB. On the contrary, dominant-negative redox-inactive mutant **thioredoxin** expression did not activate NF-kappaB, further confirming the redox-dependent activation of NF-kappaB. We also investigated the mechanism of activation of NF-kappaB by **thioredoxin** . We demonstrate that **thioredoxin** activates c-Jun NH(2)-terminal kinase (JNK)-signaling cascade, and dominant-negative expression of mitogen-activated protein kinase kinase kinase 1 (MEKK1), JNK kinase, or

JNK inhibits NF-kappaB activation by **thioredoxin** . In contrast, wild-type MEKK1 or JNK kinase induced NF-kappaB activation alone or in combination with **thioredoxin** expression plasmid. These findings were also confirmed by NF-kappaB-dependent luciferase reporter gene transcription.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Acetylcysteine--analogs and derivatives--AA; * **I-kappa B** --metabolism--ME; *Mitogen-Activated Protein Kinases--physiology--PH; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --pharmacology--PD; Acetylcysteine--pharmacology--PD; Active Transport, Cell Nucleus; Bacterial Proteins--pharmacology--PD; Cell Line; Cell Nucleus--metabolism--ME; Endothelium, Vascular--drug effects--DE; Endothelium, Vascular--metabolism --ME; Escherichia coli; Genes, Reporter; Mitogen-Activated Protein Kinase Kinases--genetics--GE; Mitogen-Activated Protein Kinase Kinases --physiology--PH; Mitogen-Activated Protein Kinases--genetics--GE; Mutation ; Oxidation-Reduction; Protein Kinase C--metabolism--ME; Protein-Serine-Threonine Kinases--genetics--GE; Protein-Serine-Threonine Kinases--physiology--PH

CAS Registry No.: 0 (Bacterial Proteins); 0 (I-kappa B); 0 (NF-kappa B); 133343-34-7 (lactacystin); 52500-60-4 (Thioredoxin); 616-91-1 (Acetylcysteine)

Enzyme No.: EC 2.7.1.- (JNK-activating protein kinase); EC 2.7.1.- (MEK kinase); EC 2.7.1.- (SAPK-ERK kinase 1); EC 2.7.1.37 (Mitogen-Activated Protein Kinase Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Protein Kinase C); EC 2.7.1.37 (Protein-Serine-Threonine Kinases); EC 2.7.10.- (c-Jun amino-terminal kinase)

Record Date Created: 20010523

Record Date Completed: 20010628

Date of Electronic Publication: 20001103

13/9/22

DIALOG(R)File 155:MEDLINE(R)

11266902 PMID: 11344124

Induction of HIF-1alpha in response to hypoxia is instantaneous.

Jewell U R; Kvietikova I; Scheid A; Bauer C; Wenger R H; Gassmann M

Institute of Physiology, University of Zurich, CH-8057 Zurich, Switzerland.

FASEB journal - official publication of the Federation of American Societies for Experimental Biology (United States) May 2001, 15 (7) p1312-4, ISSN 0892-6638 Journal Code: 8804484

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Tags: Human

Descriptors: *Cell Hypoxia--physiology--PH; *DNA-(Apurinic or Apyrimidinic Site) Lyase; *DNA-Binding Proteins--metabolism--ME; *Gene Expression Regulation; *Nuclear Proteins--metabolism--ME; *Oxygen --metabolism--ME; *Transcription Factors--metabolism--ME; Carbon-Oxygen Lyases--metabolism--ME; DNA-Binding Proteins--genetics--GE; Hela Cells; Immunoblotting; Kinetics; **NF-kappa B** --metabolism--ME; Nuclear Proteins --genetics--GE; Proto-Oncogene Proteins c-fos--metabolism--ME; Proto-Oncogene Proteins c-jun--metabolism--ME; **Thioredoxin** --metabolism --ME; Time Factors; Transcription Factors--genetics--GE

CAS Registry No.: 0 (DNA-Binding Proteins); 0 (HIF-1 protein); 0 (HIF1alpha protein); 0 (NF-kappa B); 0 (Nuclear Proteins); 0 (Proto-Oncogene Proteins c-fos); 0 (Proto-Oncogene Proteins c-jun); 0 (Transcription Factors); 52500-60-4 (Thioredoxin); 7782-44-7 (Oxygen); NM 001641 (APEX1 protein, human)

Enzyme No.: EC 4.2 (Carbon-Oxygen Lyases); EC 4.2.99.18 (DNA-(Apurinic or Apyrimidinic Site) Lyase)

Record Date Created: 20010509

Record Date Completed: 20010614

Record Date Completed: 20010517

13/9/24
DIALOG(R)File 155:MEDLINE(R)

11168529 PMID: 11165237
An endogenous redox molecule, thioredoxin **, regulates transactivation of epidermal growth factor receptor and activation of NF-kappaB by lysophosphatidic acid.**
Hirota K; Murata M; Itoh T; Yodoi J; Fukuda K
Department of Anesthesia, Kyoto University Hospital, Kyoto University, Japan. khirota@kuhp.kyoto-u.ac.jp
FEBS letters (Netherlands) Feb 2 2001, 489 (2-3) p134-8, ISSN 0014-5793 Journal Code: 0155157
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Lysophosphatidic acid (LPA) is the smallest and simplest of all the glycerophospholipids that activates a specific GTP-binding protein coupled receptor to evoke multiple cellular responses. In this paper, we have demonstrated that LPA stimulates nuclear factor (NF)-kappaB-dependent gene induction in a neuronal cell line, NG108-15 and that this is under redox regulation by an endogenous molecule, **thioredoxin** . We also have shown that redox-sensitive transactivation of epidermal growth factor receptor by LPA confers NF-kappaB activation and small GTPase proteins are involved in this pathway.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: Lysophospholipids--pharmacology--PD; * **NF-kappa B** --drug effects--DE; *Receptor, Epidermal Growth Factor--metabolism--ME; * **Thioredoxin** --metabolism--ME; Animals; Cell Line; DNA, Recombinant; Dose-Response Relationship, Drug; Heterotrimeric GTP-Binding Proteins --genetics--GE; Heterotrimeric GTP-Binding Proteins--metabolism--ME; Hybrid Cells; Luciferase--genetics--GE; Luciferase--metabolism--ME; Monomeric GTP-Binding Proteins--genetics--GE; Monomeric GTP-Binding Proteins--metabolism--ME; **NF-kappa B** --metabolism--ME; Oxidation-Reduction ; Plasmids--genetics--GE; Receptor, Epidermal Growth Factor--genetics--GE; Recombinant Fusion Proteins--drug effects--DE; Recombinant Fusion Proteins --genetics--GE; Recombinant Fusion Proteins--metabolism--ME; **Thioredoxin** --genetics--GE; Trans-Activation (Genetics)--drug effects--DE; Tumor Cells, Cultured
CAS Registry No.: 0 (DNA, Recombinant); 0 (Lysophospholipids); 0 (NF-kappa B); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 1.13.12.- (Luciferase); EC 2.7.1.112 (Receptor, Epidermal Growth Factor); EC 3.6.1.- (Monomeric GTP-Binding Proteins); EC 3.6.1.46 (Heterotrimeric GTP-Binding Proteins)
Record Date Created: 20010222
Record Date Completed: 20010315

13/9/25
DIALOG(R)File 155:MEDLINE(R)

11136841 PMID: 11134546
The activity of NF-kappaB in Swiss 3T3 cells exposed to aqueous extracts of cigarette smoke is dependent on thioredoxin .
Gebel S; Muller T
INBIFO Institut fur biologische Forschung, Fuggerstr.3, D-51149 Koln, Germany.
Toxicological sciences - an official journal of the Society of Toxicology (United States) Jan 2001, 59 (1) p75-81, ISSN 1096-6080 Journal Code: 9805461

Comment on Toxicol Sci. 2001 Jan;59(1) 75-81; Comment on PMID 11134546; Comment in Toxicol Sci. 2001 Jan;59(1):1-2; Comment in PMID 11134538; Comment in Toxicol Sci. 2001 Jan;59(1):75-81; Comment in PMID 11134546
Document type: Comment; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Multiple studies in vitro have demonstrated that aqueous extracts of mainstream cigarette smoke (CS) [smoke-bubbled phosphate-buffered saline (PBS)] induce a distinct pattern of stress response in cultured cells, which may be related to the reported pro-inflammatory activities of CS in vitro and in vivo. Nuclear factor kappaB (NF-kappaB) is a transcription factor involved in both inflammatory and stress-dependent cell-signaling processes. Here we report on the activity of NF-kappaB in cells exposed to subcytotoxic concentrations of smoke-bubbled PBS. Using electrophoretic mobility shift assay (EMSA) techniques, we observed a decreased DNA binding of NF-kappaB during the first 2 h of exposure, which was followed by a more than 2-fold increase over controls after 4 to 6 h of exposure. This type of kinetics is not regulated by IkappaB-alpha, as evidenced by the lack of phosphorylation and degradation of IkappaB-alpha in CS-treated cells. However, as demonstrated in immuno-coprecipitation experiments, the kinetics of NF-kappaB DNA binding is strictly paralleled by decreased and increased complex formation between NF-kappaB and **thioredoxin** (Trx), the reducing catalyst of Cys-62 of NF-kappaB subunit p50, the reduced thiol function of which is essential for efficient NF-kappaB DNA binding. Monitoring the expression of the gene encoding **thioredoxin** reductase (TrxR), which is required to keep Trx in a functional reduced state, we observed a significant increase in TrxR mRNA after 2 to 6 h of exposure. Based on the correspondence between the kinetics of NF-kappaB DNA binding, NF-kappaB/Trx complex formation, and TrxR expression, along with a lack of IkappaB-alpha phosphorylation and degradation, these results suggest that the activity of NF-kappaB in CS-treated cells is subject mainly to a redox-controlled mechanism dependent on the availability of reduced Trx rather than being controlled by its normal regulator, IkappaB-alpha.

Tags: Support, Non-U.S. Gov't
Descriptors: 3T3 Cells--metabolism--ME; * **I-kappa B** ; * **NF-kappa B** --metabolism--ME; *Plants, Toxic; *Smoke--adverse effects--AE; * **Thioredoxin** --metabolism--ME; *Tobacco; *Transcription, Genetic--drug effects--DE; 3T3 Cells--drug effects--DE; Animals; Blotting, Western; DNA --drug effects--DE; DNA--metabolism--ME; DNA Primers--analysis--AN; DNA-Binding Proteins--genetics--GE; DNA-Binding Proteins--metabolism--ME; Electrophoresis, Polyacrylamide Gel; Glutathione--metabolism--ME; In Situ Hybridization; Mice; **NF-kappa B** --antagonists and inhibitors--AI; **NF-kappa B** --genetics--GE; RNA--isolation and purification--IP; RNA --metabolism--ME; Reverse Transcriptase Polymerase Chain Reaction; **Thioredoxin** --genetics--GE; **Thioredoxin** Reductase (NADPH)--genetics--GE; **Thioredoxin** Reductase (NADPH)--metabolism--ME
CAS Registry No.: 0 (DNA Primers); 0 (DNA-Binding Proteins); 0 (I-kappa B); 0 (NF-kappa B); 139874-52-5 (NF-kappaB inhibitor alpha); 52500-60-4 (Thioredoxin); 63231-63-0 (RNA); 70-18-8 (Glutathione); 9007-49-2 (DNA)
Enzyme No.: EC 1.6.4.5 (**Thioredoxin** Reductase (NADPH))
Record Date Created: 20010126
Record Date Completed: 20010222

13/9/26
DIALOG(R)File 155:MEDLINE(R)

11101148 PMID: 11126428
Nutrition, HIV, and drug abuse: the molecular basis of a unique role for selenium.
Taylor E W; Cox A G; Zhao L; Ruzicka J A; Bhat A A; Zhang W; Nadimpalli R G; Dean R G
Department of Pharmaceutical and Biomedical Sciences and Computational

Center for Molecular Structure and Design, The University of Georgia, Athens 30602, USA. wtaylor@rx.uga.edu
Journal of acquired immune deficiency syndromes (1999) (United States) Oct 1 2000, 25 Suppl 1 pS53-61, ISSN 1525-4135 Journal Code: 100892005
Contract/Grant No.: RO1 DA11378; DA; NIDA
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

HIV-infected injection drug users (IDUs) often suffer from serious nutritional deficiencies. This is a concern because plasma levels of micronutrients such as vitamin B12, zinc, and selenium have been correlated with mortality risk in HIV-positive populations. Injection drug use also increases lipid peroxidation and other indicators of oxidative stress, which, combined with antioxidant deficiencies, can stimulate HIV-1 replication through activation of NF-kappaB transcription factors, while weakening immune defenses. As detailed herein, these prooxidant stimuli can also increase the pathogenic effects of HIV-1 by another mechanism, involving viral selenoproteins. Overlapping the envelope coding region, HIV-1 encodes a truncated glutathione peroxidase (GPx) gene (see #6 in reference list). Sequence analysis and molecular modeling show that this viral GPx (vGPx) module has highly significant structural similarity to known mammalian GPx, with conservation of the catalytic triad of selenocysteine (Sec), glutamine, and tryptophan. In addition to other functions, HIV-1 vGPx may serve as a negative regulator of proviral transcription, by acting as an NF-kappaB inhibitor (a known property of cellular GPx). Another potential selenoprotein coding function of HIV-1 is associated with the 3' end of the nef gene, which terminates in a conserved UGA (potential Sec) codon in the context of a sequence (Cys-Sec) identical to the C-terminal redox center of **thioredoxin** reductase, another cellular regulator of NF-kappaB. Thus, in combination with known cellular mechanisms involving Se, viral selenoproteins may represent a unique mechanism by which HIV-1 monitors and exploits an essential micronutrient to optimize its replication relative to the host. (35 Refs.)

Tags: Human; Support, U.S. Gov't, P.H.S.
Descriptors: *Glutathione Peroxidase--genetics--GE; *HIV Infections --complications--CO; *HIV Infections--virology--VI; *HIV-1--genetics--GE; *Selenium--metabolism--ME; *Substance Abuse, Intravenous--complications--CO ; Amino Acid Sequence; Disease Progression; Glutathione Peroxidase --chemistry--CH; Glutathione Peroxidase--metabolism--ME; HIV Infections --physiopathology--PP; HIV-1--chemistry--CH; HIV-1--enzymology--EN; Models, Molecular; Molecular Sequence Data; **NF-kappa B** --chemistry--CH; **NF-kappa B** --genetics--GE; **NF-kappa B** --metabolism--ME; Nutrition; Substance Abuse, Intravenous--physiopathology--PP; **Thioredoxin** Reductase (NADPH)--chemistry--CH; **Thioredoxin** Reductase (NADPH)--genetics--GE; **Thioredoxin** Reductase (NADPH)--metabolism--ME; Transcription, Genetic
CAS Registry No.: 0 (NF-kappa B); 7782-49-2 (Selenium)
Enzyme No.: EC 1.11.1.9 (Glutathione Peroxidase); EC 1.6.4.5 (**Thioredoxin** Reductase (NADPH))
Record Date Created: 20001220
Record Date Completed: 20010111

13/9/27
DIALOG(R)File 155:MEDLINE(R)

10846919 PMID: 10973806
Geranylgeranylacetone enhances expression of thioredoxin **and suppresses ethanol-induced cytotoxicity in cultured hepatocytes.**
Hirota K; Nakamura H; Arai T; Ishii H; Bai J; Itoh T; Fukuda K; Yodoi J
Department of Anesthesia, Kyoto University Hospital, Kyoto University, 54 Shogoin-Kawaharacho, Kyoto, Sakyo-Ku, 606-8507, Japan. khirota@kuhp.kyoto-u .ac.jp
Biochemical and biophysical research communications (UNITED STATES) Sep 7 2000, 275 (3) p825-30, ISSN 0006-291X Journal Code: 0372516

intracellularly generated H(2)O(2) has a role in transcription factor activation by both TNF-alpha and IL-1beta.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *Cytokines--metabolism--ME; *Reactive Oxygen Species --metabolism--ME; *Selenium--pharmacology--PD; *Signal Transduction--drug effects--DE; Biphenyl Compounds--pharmacology--PD; Cell Line; Enzyme Inhibitors--pharmacology--PD; Genes, Reporter; Glutathione--metabolism--ME; Hydrogen Peroxide--metabolism--ME; Interleukin-1--pharmacology--PD; NADPH Oxidase--antagonists and inhibitors--AI; **NF-kappa B** --metabolism--ME; Onium Compounds--pharmacology--PD; Peroxidases--metabolism--ME; Superoxides --metabolism--ME; **Thioredoxin** Reductase (NADPH)--metabolism--ME; Trans-Activation (Genetics)--drug effects--DE; Tumor Necrosis Factor --pharmacology--PD
CAS Registry No.: 0 (Biphenyl Compounds); 0 (Cytokines); 0 (Enzyme Inhibitors); 0 (Interleukin-1); 0 (NF-kappa B); 0 (Onium Compounds); 0 (Reactive Oxygen Species); 0 (Tumor Necrosis Factor); 10182-84-0 (diphenyliodonium); 11062-77-4 (Superoxides); 70-18-8 (Glutathione); 7722-84-1 (Hydrogen Peroxide); 7782-49-2 (Selenium)
Enzyme No.: EC 1.11.1. (Peroxidases); EC 1.6.- (NADPH Oxidase); EC 1.6.4.5 (**Thioredoxin** Reductase (NADPH))
Record Date Created: 20000802
Record Date Completed: 20000802

13/9/30
DIALOG(R)File 155:MEDLINE(R)

10671217 PMID: 10781815
Upregulation of thioredoxin **(TRX) expression in giant cell myocarditis in rats.**
Shioji K; Kishimoto C; Nakamura H; Toyokuni S; Nakayama Y; Yodoi J; Sasayama S
Department of Cardiovascular Medicine, Graduate School of Medicine, Kyoto University, 54 Kawaracho, Shogoin, Sakyo-ku, Kyoto, Japan.
FEBS letters (NETHERLANDS) Apr 21 2000, 472 (1) p109-13, ISSN 0014-5793 Journal Code: 0155157
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
To examine the possible involvement of a redox regulating mechanism in the pathogenesis of immune-mediated myocarditis, myocarditis was induced by immunization of porcine cardiac myosin in rats and immunohistochemistry and Western blot for **thioredoxin** (TRX) were performed. Immunohistochemistry for 8-hydroxy-2'-deoxyguanosine (8-OHdG) and nuclear factor kappa-B (NF-kappaB) was also performed. TRX was upregulated in the acute stage, but not in the chronic stage, and the expression was correlated with the severity of the disease. Damaged myocytes were strongly immunostained for 8-OHdG and NF-kappaB. Thus, TRX may be specifically induced by acute inflammatory stimuli, and the development of acute immune-mediated myocarditis may be regulated by the cellular redox state via TRX.
Descriptors: Giant Cells--metabolism--ME; *Myocarditis--metabolism--ME; * **Thioredoxin** --metabolism--ME; Animals; Blotting, Western; Deoxyguanosine --analogs and derivatives--AA; Deoxyguanosine--metabolism--ME; Giant Cells --pathology--PA; Immunohistochemistry; Myocarditis--immunology--IM; Myocarditis--pathology--PA; Myocardium--chemistry--CH; Myocardium --pathology--PA; Myosins--chemistry--CH; Myosins--immunology--IM; **NF-kappa B** --metabolism--ME; Oxidation-Reduction; Rats; Rats, Inbred Lew; Swine; **Thioredoxin** --genetics--GE; Vaccination
CAS Registry No.: 0 (8-hydroxy-2'-deoxyguanosine); 0 (NF-kappa B); 52500-60-4 (Thioredoxin); 961-07-9 (Deoxyguanosine)
Enzyme No.: EC 3.6.1.4 (Myosins)
Record Date Created: 20000602
Record Date Completed: 20000602

13/9/31
DIALOG(R)File 155:MEDLINE(R)

10638702 PMID: 10745031

A novel mechanism of retinoic acid-enhanced interleukin-8 gene expression in airway epithelium.

Chang M M; Harper R; Hyde D M; Wu R

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American journal of respiratory cell and molecular biology (UNITED STATES) Apr 2000, 22 (4) p502-10, ISSN 1044-1549 Journal Code: 8917225

Contract/Grant No.: ES00628; ES; NIEHS; ES06230; ES; NIEHS; HL35635; HL; NHLBI; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A 3- to 8-fold stimulation of interleukin (IL)-8 gene expression by all-trans-retinoic acid (ATRA) was demonstrated in primary cultures of human and monkey tracheobronchial epithelial cells and BEAS-2B serum-sensitive cell line. The effect of ATRA on IL-8 gene expression is dose- and time-dependent. Using cycloheximide, it was observed that new protein synthesis was required for the stimulation. ATRA had no effect on IL-8 messenger RNA stability. A difference in nuclear run-on activity suggests that a transcriptional mechanism is involved in ATRA-enhanced IL-8 gene expression. Promoter-reporter gene transfection studies demonstrated ATRA enhanced IL-8 promoter activity, especially when cells were cotransfected with retinoic acid nuclear receptor-alpha expression vector. Deletion and site-directed mutagenesis analysis revealed the involvement of nuclear factor (NF)-kappaB binding site of the IL-8 gene in ATRA-enhanced promoter activity. Electrophoretic mobility shift assay (EMSA) demonstrated that ATRA enhanced DNA-NF-kappaB complex formation, especially with the p65 subunit. Western blot analysis demonstrated that ATRA did not enhance the protein amount of both the p50 and the p65 subunits in the nuclei. Because ATRA also enhances **thioredoxin** (TRX) gene expression, the effect of TRX on IL-8 gene expression was examined. IL-8 promoter activity was enhanced in transfected cells by the addition of TRX protein. Treatment of nuclear extracts with TRX also enhanced DNA- NF-kappaB complex formation as observed by EMSA, particularly the p65 subunit. Taking these data together, a novel mechanism is proposed in which ATRA activates promoter activity of IL-8 gene through TRX-dependent NF-kappaB activation.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Bronchi--drug effects--DE; *Gene Expression Regulation --drug effects--DE; *Interleukin-8--biosynthesis--BI; *Trachea --drug effects--DE; *Tretinoin--pharmacology--PD; Animals; Bronchi--metabolism--ME ; Consensus Sequence; Cycloheximide--pharmacology--PD; Dactinomycin --pharmacology--PD; Epithelium--drug effects--DE; Epithelium--metabolism --ME; Interleukin-8--genetics--GE; Macaca mulatta; Mutagenesis, Site-Directed; **NF-kappa B** --physiology--PH; Nucleic Acid Synthesis Inhibitors--pharmacology--PD; Protein Synthesis Inhibitors--pharmacology --PD; RNA, Messenger--metabolism--ME; Sequence Deletion; **Thioredoxin** --biosynthesis--BI; Trachea--metabolism--ME; Transcription, Genetic--drug effects--DE; Transfection

CAS Registry No.: 0 (Interleukin-8); 0 (NF-kappa B); 0 (Nucleic Acid Synthesis Inhibitors); 0 (Protein Synthesis Inhibitors); 0 (RNA, Messenger); 302-79-4 (Tretinoin); 50-76-0 (Dactinomycin); 52500-60-4 (Thioredoxin); 66-81-9 (Cycloheximide)

Record Date Created: 20000524

Record Date Completed: 20000524

13/9/32
DIALOG(R)File 155:MEDLINE(R)

10535198 PMID: 10636891

Inhibition of the c-Jun N-terminal kinase/AP-1 and NF-kappaB pathways by PICOT, a novel protein kinase C-interacting protein with a thioredoxin **homology domain.**

Witte S; Villalba M; Bi K; Liu Y; Isakov N; Altman A

Division of Cell Biology, La Jolla Institute for Allergy and Immunology, San Diego, California 92121, USA.

Journal of biological chemistry (UNITED STATES) Jan 21 2000, 275 (3) p1902-9, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: CA35299; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Protein kinase C-theta (PKCtheta) is a Ca(2+)-independent PKC isoform that is selectively expressed in T lymphocytes (and muscle), and is thought to play an important role in T cell receptor-induced activation. To gain a better understanding of the function and regulation of PKCtheta, we have employed the yeast two-hybrid system to identify PKCtheta-interacting proteins. We report the isolation and characterization of a cDNA encoding a novel 335-amino acid (37. 5-kDa) PKCtheta-interacting protein termed PICOT (for PKC-interacting cousin of **thioredoxin**). PICOT is expressed in various tissues, including in T cells, where it colocalizes with PKCtheta. PICOT displays an N-terminal **thioredoxin** homology domain, which is required for the interaction with PKC. Comparison of the unique C-terminal region of PICOT with expressed sequence tag data bases revealed two tandem repeats of a novel domain that is highly conserved from plants to mammals. Transient overexpression of full-length PICOT (but not its N- or C-terminal fragments) in T cells inhibited the activation of c-Jun N-terminal kinase (but not extracellular signal-regulated kinase), and the transcription factors AP-1 or NF-kappaB. These findings suggest that PICOT and its evolutionary conserved homologues may interact with PKC-related kinases in multiple organisms and, second, that it plays a role in regulating the function of the **thioredoxin** system.

Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: Carrier Proteins--chemistry--CH; *Carrier Proteins --physiology--PH; *Mitogen-Activated Protein Kinases --antagonists and inhibitors--AI; * **NF-kappa B** --antagonists and inhibitors--AI; *Protein Kinase C--metabolism--ME; * **Thioredoxin** --metabolism--ME; *Transcription Factor AP-1--antagonists and inhibitors--AI; Amino Acid Sequence; Carrier Proteins--pharmacology--PD; Glutathione Transferase--metabolism--ME; Jurkat Cells; Lymphocyte Activation--physiology--PH; MAP Kinase Signaling System --drug effects--DE; Molecular Sequence Data; Plasmids; Protein Binding; Recombinant Fusion Proteins--metabolism--ME; Reverse Transcriptase Polymerase Chain Reaction; Sequence Homology, Amino Acid; T-Lymphocytes --drug effects--DE; Transfection; Two-Hybrid System Techniques

CAS Registry No.: 0 (Carrier Proteins); 0 (MAP Kinase Signaling System); 0 (NF-kappa B); 0 (PICOT protein); 0 (Plasmids); 0 (Recombinant Fusion Proteins); 0 (Transcription Factor AP-1); 52500-60-4 (Thioredoxin)

Enzyme No.: EC 2.5.1.18 (Glutathione Transferase); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (Protein Kinase C); EC 2.7.10.- (c-Jun amino-terminal kinase)

Record Date Created: 20000224

Record Date Completed: 20000224

13/9/33

10487492 PMID: 10586691

[Biological response to oxidative stress and the signal transduction pathway of NF-kappa B]

Okamoto T

Department of Molecular Genetics, Nagoya City University Medical School, Japan. tokamoto@med.nagoya-cu.ac.jp
Tanpakushitsu kakusan koso. Protein, nucleic acid, enzyme (JAPAN) Nov 1999, 44 (15 Suppl) p2405-13, ISSN 0039-9450 Journal Code: 0413762
Document type: Journal Article; Review; Review, Tutorial
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
(40 Refs.)
Descriptors: **NF-kappa B** --physiology--PH; *Oxidative Stress; *Signal Transduction--physiology--PH; Animals; Glutathione--physiology--PH; **NF-kappa B** --metabolism--ME; Oxidation-Reduction; Oxidoreductases --physiology--PH; Phosphorylation; Protein-Serine-Threonine Kinases; Reactive Oxygen Species--physiology--PH; **Thioredoxin**
CAS Registry No.: 0 (NF-kappa B); 0 (Reactive Oxygen Species); 52500-60-4 (Thioredoxin); 70-18-8 (Glutathione)
Enzyme No.: EC 1. (Oxidoreductases); EC 1.8.4.1 (thioltransferase); EC 2.7.1.- (NF-kappa B kinase); EC 2.7.1.37 (Protein-Serine-Threonine Kinases)
Record Date Created: 20000217
Record Date Completed: 20000217

13/9/34
DIALOG(R)File 155:MEDLINE(R)

10487491 PMID: 10586690
[Oxy-stress response and its control mechanism: overview]
Okamoto T
Department of Molecular Genetics, Nagoya City University Medical School, Japan. tokamoto@med.nagoya-cu.ac.jp
Tanpakushitsu kakusan koso. Protein, nucleic acid, enzyme (JAPAN) Nov 1999, 44 (15 Suppl) p2403-4, ISSN 0039-9450 Journal Code: 0413762
Document type: Journal Article; Review; Review, Tutorial
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
(0 Refs.)
Descriptors: **NF-kappa B** --physiology--PH; *Oxidative Stress; Oxidation-Reduction; Phosphorylation; Protein-Tyrosine Kinase--physiology --PH; Signal Transduction--physiology--PH; **Thioredoxin** ; Transcription Factor AP-1--physiology--PH
CAS Registry No.: 0 (NF-kappa B); 0 (Transcription Factor AP-1); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 2.7.1.- (protein tyrosine kinase brk, human); EC 2.7.1.112 (Protein-Tyrosine Kinase)
Record Date Created: 20000217
Record Date Completed: 20000217

13/9/35
DIALOG(R)File 155:MEDLINE(R)

10469946 PMID: 10569626
Gene expression and the thiol redox state.
Arrigo A P
Laboratoire du Stress Cellulaire, Centre de Genetique Moleculaire et Cellulaire, CNRS-UMR-5534, Universite Claude Bernard LYON-I, Villeurbanne, France. arrigo@univ-lyon1.fr
Free radical biology & medicine (UNITED STATES) Nov 1999, 27 (9-10) p936-44, ISSN 0891-5849 Journal Code: 8709159
Document type: Journal Article; Review; Review, Academic
Languages: ENGLISH

Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The intracellular redox status is a tightly regulated parameter which provides the cell with an optimal ability to counteract the highly oxidizing extracellular environment. Intracellular redox homeostasis is regulated by thiol-containing molecules, such as glutathione and **thioredoxin** . Essential cellular functions, such as gene expression, are influenced by the balance between pro- and antioxidant conditions. The mechanism by which the transcription of specific eukaryotic genes is redox regulated is complex, however, recent findings suggest that redox-sensitive transcription factors play an essential role in this process. This review is focused on the recent knowledge concerning some eukaryotic transcription factors, whose activation and DNA binding is controlled by the thiol redox status of the cell. (104 Refs.)

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Gene Expression Regulation; *Sulfhydryl Compounds --metabolism--ME; Animals; DNA-Binding Proteins--metabolism--ME; Genes, fos ; Genes, jun; Homeostasis; **NF-kappa B** --metabolism--ME; Oxidation-Reduction; Protein p53--metabolism--ME; Transcription Factor AP-1 --metabolism--ME; Transcription Factors--metabolism--ME

CAS Registry No.: 0 (DNA-Binding Proteins); 0 (NF-kappa B); 0 (Protein p53); 0 (Sulfhydryl Compounds); 0 (Transcription Factor AP-1) ; 0 (Transcription Factors); 136111-36-9 (heat shock factor, human)

Record Date Created: 19991222
Record Date Completed: 19991222

13/9/36

DIALOG(R)File 155:MEDLINE(R)

10258360 PMID: 7958618

Functions of glutathione and glutathione disulfide in immunology and immunopathology.

Droge W; Schulze-Osthoff K; Mihm S; Galter D; Schenk H; Eck H P; Roth S; Gmunder H

Department of Immunochemistry, Deutsches Krebsforschungszentrum, Heidelberg, Germany.

FASEB journal - official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Nov 1994, 8 (14) p1131-8, ISSN 0892-6638 Journal Code: 8804484

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

Even a moderate increase in the cellular cysteine supply elevates the intracellular glutathione (GSH) and glutathione disulfide (GSSG) levels and potentiates immunological functions of lymphocytes in vitro. At low GSSG levels, T cells cannot optimally activate the immunologically important transcription factor NF kappa B, whereas high GSSG levels inhibit the DNA binding activity of NF kappa B. The effects of GSSG are antagonized by reduced **thioredoxin** (TRX). As the protein tyrosine kinase activities p56lck and p59fyn are activated in intact cells by hydrogen peroxide, they are likely targets for GSSG action. These redox-regulated enzymes trigger signal cascades for NF kappa B activation and transduce signals from the T cell antigen receptor, from CD4 and CD8 molecules, and from the IL-2 receptor beta-chain. The effector phase of cytotoxic T cell responses and IL-2-dependent functions are inhibited even by a partial depletion of the intracellular GSH pool. As signal transduction is facilitated by prooxidant conditions, we propose that the well-known immunological consequences of GSH depletion ultimately may be results of the accompanying GSSG deficiency. As HIV-infected patients and SIV-infected rhesus macaques have, on the average, significantly decreased plasma cyst(e)ine and intracellular GSH levels, we also hypothesize that AIDS may be the consequence of a GSSG deficiency as well. (79 Refs.)

Tags: Human
Descriptors: *Glutathione--analogs and derivatives--AA; *Glutathione --physiology--PH; *T-Lymphocytes--immunology--IM; Amino Acid Sequence; Animals; Cytokines--physiology--PH; DNA-Binding Proteins--antagonists and inhibitors--AI; Glutathione Disulfide; Hydrogen Peroxide--pharmacology--PD; Immunotherapy; Molecular Sequence Data; **NF-kappa B** --physiology--PH; Neoplasms--therapy--TH; Oxidation-Reduction; Signal Transduction; T-Lymphocytes--drug effects--DE; Transcription Factor AP-1--metabolism--ME; Vaccination
CAS Registry No.: 0 (Cytokines); 0 (DNA-Binding Proteins); 0 (NF-kappa B); 0 (Transcription Factor AP-1); 27025-41-8 (Glutathione Disulfide); 70-18-8 (Glutathione); 7722-84-1 (Hydrogen Peroxide)
Record Date Created: 19941215
Record Date Completed: 19941215

13/9/37
DIALOG(R)File 155:MEDLINE(R)

10167118 PMID: 8056331
Two different cellular redox systems regulate the DNA-binding activity of the p50 subunit of NF-kappa B in vitro.
Mitomo K; Nakayama K; Fujimoto K; Sun X; Seki S; Yamamoto K
Department of Molecular Pathology, Cancer Research Institute, Kanazawa University, Ishikawa, Japan.
Gene (NETHERLANDS) Aug 5 1994, 145 (2) p197-203, ISSN 0378-1119 Journal Code: 7706761
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The NF-kappa B/Rel/Dorsal (NRD) transcription factor family binds target DNA sequences through their conserved N-terminal basic region that contains a single cysteine residue flanked by basic residues. This cysteine residue plays a critical role in the regulation of the DNA-binding activity of NRD members, since chemical modifications of this residue modulate the DNA-binding activity of NRD members. Here we show that cellular factors regulate the DNA-binding activity of NRD members in vitro by reduction-oxidation (redox) mechanisms. Two cellular redox systems, **thioredoxin** / **thioredoxin** reductase and apurinic/apyrimidinic endonuclease (also called Redox factor-1), independently, as well as, synergistically stimulate the DNA-binding activity of bacterially synthesized (recombinant) p50, one of the subunits of NF-kappa B that is a major NRD factor inducible in various types of cells. Since the mutation of the conserved residue (Cys61) in the N-terminal basic region of p50 impairs the stimulation of p50 DNA-binding activity by these redox factors, the regulation of p50 DNA-binding activity by these redox factors is mediated through this cysteine residue. It is, therefore, possible that these two cellular redox systems could play independent, as well as synergistic roles in the regulation of NF-kappa B functions in vivo through the redox control of their DNA-binding activity.
Tags: Comparative Study
Descriptors: Carbon-Oxygen Lyases; *DNA--metabolism--ME; *DNA-(Apurinic or Apyrimidinic Site) Lyase; * **NF-kappa B** --metabolism--ME; Amino Acid Sequence; Base Sequence; Molecular Sequence Data; Nuclear Proteins --metabolism--ME; Oxidation-Reduction; Protein Binding; Protein Conformation; Proto-Oncogene Proteins--metabolism--ME; Proto-Oncogene Proteins c-rel; Structure-Activity Relationship; **Thioredoxin** --metabolism --ME; **Thioredoxin** Reductase (NADPH)--metabolism--ME
CAS Registry No.: 0 (NF-kappa B); 0 (Nuclear Proteins); 0 (Proto-Oncogene Proteins); 0 (Proto-Oncogene Proteins c-rel); 52500-60-4 (Thioredoxin); 9007-49-2 (DNA); NM 001641 (APEX1 protein, human)
Enzyme No.: EC 1.6.4.5 (**Thioredoxin** Reductase (NADPH)); EC 4.2 (Carbon-Oxygen Lyases); EC 4.2.99.18 (DNA-(Apurinic or Apyrimidinic Site) Lyase)

Record Date Created: 19940915
Record Date Completed: 19940915

13/9/38
DIALOG(R)File 155:MEDLINE(R)

10062654 PMID: 8174544
Distinct effects of glutathione disulphide on the nuclear transcription factor kappa B and the activator protein-1.
Galter D; Mihm S; Droge W
Division of Immunochemistry, Deutsches Krebsforschungszentrum, Heidelberg, Germany.
European journal of biochemistry / FEBS (GERMANY) Apr 15 1994, 221 (2) p639-48, ISSN 0014-2956 Journal Code: 0107600
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Oxidative conditions potentiate the activation of the nuclear transcription factor kappa B (NF kappa B) and the activator protein-1 (AP-1) in intact cells, but inhibit their DNA binding activity in vitro. We now show that both the activation of NF kappa B and the inhibition of its DNA binding activity is modulated in intact cells by the physiological oxidant glutathione disulphide (GSSG). NF kappa B activation in human T lineage cells (Molt-4) by 12-O-tetradecanoyl-phorbol 13-acetate was inhibited by dithiothreitol, and this was partly reversed by the glutathione reductase inhibitor 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) or by hydrogen peroxide, indicating that GSSG may be required for NF kappa B activation. These effects of BCNU and hydrogen peroxide were not seen in glutathione-depleted cells. However, NF kappa B and AP-1 activation were potentiated by dithiothreitol if added to cell cultures 1 h after the phorbol ester, indicating that a shift of redox conditions may support optimal oxidative activation with minimal inhibition of DNA binding. The elevation of intracellular GSSG levels by BCNU before stimulation suppressed the chloramphenicol acetyltransferase expression dependent on NF kappa B but increased that dependent on AP-1. This selective suppression of NF kappa B was also demonstrable by electrophoretic mobility shift assays. In vitro, GSSG inhibited the DNA binding activity of NF kappa B more effectively than that of AP-1, while AP-1 was inhibited more effectively by oxidized **thioredoxin** .
Descriptors: DNA--metabolism--ME; *DNA-Binding Proteins--metabolism--ME; *Glutathione--analogs and derivatives--AA; *Homeodomain Proteins; * **NF-kappa B** --metabolism--ME; *Proto-Oncogene Proteins c-bcl-2; *Repressor Proteins; *Saccharomyces cerevisiae Proteins; *T-Lymphocytes--metabolism --ME; *Transcription, Genetic; Animals; Antioxidants--pharmacology--PD; Base Sequence; Carmustine--pharmacology--PD; Cell Line; Chloramphenicol O-Acetyltransferase--genetics--GE; Glutathione--metabolism--ME; Glutathione Disulfide; Hydrogen Peroxide--pharmacology--PD; Molecular Sequence Data; Oxidation-Reduction; Pyrrolidines--pharmacology--PD; T-Lymphocytes --drug effects--DE; Tetradecanoylphorbol Acetate--pharmacology--PD; Thiocarbamates --pharmacology--PD; **Thioredoxin** --pharmacology--PD; Transcription, Genetic --drug effects--DE
CAS Registry No.: 0 (Antioxidants); 0 (BCL2A1 protein); 0 (DNA-Binding Proteins); 0 (Homeodomain Proteins); 0 (MATA1 protein, S cerevisiae); 0 (NF-kappa B); 0 (Proto-Oncogene Proteins c-bcl-2); 0 (Pyrrolidines); 0 (Repressor Proteins); 0 (Saccharomyces cerevisiae Proteins); 0 (Thiocarbamates); 0 (activator 1 protein); 154-93-8 (Carmustine); 16561-29-8 (Tetradecanoylphorbol Acetate); 25769-03-3 (pyrrolidine dithiocarbamic acid); 27025-41-8 (Glutathione Disulfide); 52500-60-4 (Thioredoxin); 70-18-8 (Glutathione); 7722-84-1 (Hydrogen Peroxide); 9007-49-2 (DNA)
Enzyme No.: EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase)
Record Date Created: 19940609
Record Date Completed: 19940609

13/9/39
DIALOG(R)File 155:MEDLINE(R)

10007763 PMID: 8127864
Distinct effects of thioredoxin **and antioxidants on the activation of transcription factors NF-kappa B and AP-1.**
Schenk H; Klein M; Erdbrugger W; Droge W; Schulze-Osthoff K
Division of Immunochemistry, Deutsches Krebsforschungszentrum, Heidelberg, Federal Republic of Germany.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Mar 1 1994, 91 (5) p1672-6, ISSN 0027-8424
Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The transcription factors NF-kappa B and AP-1 have been implicated in the inducible expression of a variety of genes involved in responses to oxidative stress and cellular defense mechanisms. Here, we report that **thioredoxin** , an important cellular protein oxidoreductase with antioxidant activity, exerts different effects on the activation of NF-kappa B and AP-1. Transient expression or exogenous application of **thioredoxin** resulted in a dose-dependent inhibition of NF-kappa B activity, as demonstrated in gel shift and transactivation experiments. AP-1-dependent transactivation, in contrast was strongly enhanced by **thioredoxin** . A similar increase of AP-1 activity was also observed with other, structurally unrelated antioxidants such as pyrrolidine dithiocarbamate and butylated hydroxyanisole, indicating that the **thioredoxin** -induced increase of AP-1 activation was indeed based on an antioxidant effect. Moreover, the stimulatory effect on AP-1 activity was found to involve de novo transcription of the c-jun and c-fos components but to be independent of protein kinase C activation. These results suggest that **thioredoxin** plays an important role in the regulation of transcriptional processes and oppositely affects NF-kappa B and AP-1 activation.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: Antioxidants--pharmacology--PD; * **NF-kappa B** --metabolism --ME; *Proto-Oncogene Proteins c-jun--metabolism--ME; * **Thioredoxin** --pharmacology--PD; Animals; Base Sequence; Cell Line; DNA Probes--genetics --GE; Genes, fos--drug effects--DE; Genes, jun--drug effects--DE; Hela Cells; Mice; Molecular Sequence Data; **NF-kappa B** --genetics--GE; Proto-Oncogene Proteins c-jun--genetics--GE; Pyrrolidines--pharmacology--PD ; Recombinant Fusion Proteins--pharmacology--PD; Tetradecanoylphorbol Acetate--pharmacology--PD; Thiocarbamates--pharmacology--PD; **Thioredoxin** --biosynthesis--BI; **Thioredoxin** --genetics--GE; Trans-Activation (Genetics)--drug effects--DE
CAS Registry No.: 0 (Antioxidants); 0 (DNA Probes); 0 (NF-kappa B); 0 (Proto-Oncogene Proteins c-jun); 0 (Pyrrolidines); 0 (Recombinant Fusion Proteins); 0 (Thiocarbamates); 16561-29-8 (Tetradecanoylphorbol Acetate); 25769-03-3 (pyrrolidine dithiocarbamic acid); 52500-60-4 (Thioredoxin)
Gene Symbol: c-fos; c-jun
Record Date Created: 19940411
Record Date Completed: 19940411

13/9/40
DIALOG(R)File 155:MEDLINE(R)

09711012 PMID: 8496188
Oxidoreductive regulation of nuclear factor kappa B. Involvement of a cellular reducing catalyst thioredoxin .

Hayashi T; Ueno Y; Okamoto T
Virology Division, National Cancer Center Research Institute, Tokyo, Japan.
Journal of biological chemistry (UNITED STATES) May 25 1993, 268 (15) p11380-8, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS; AIDS/HIV

We have investigated an oxidoreductive regulatory pathway for the DNA binding activity of a pleiotropic cellular transcription factor, nuclear factor kappa B (NF kappa B), has been investigated by using NF kappa B prepared from the nucleus and the cytosol of the primary human T lymphocytes. We show that a cellular reducing catalyst **thioredoxin** (Trx) plays a major role in activation of the DNA binding of NF kappa B in vitro and stimulation of transcription from the NF kappa B-dependent gene expression. We demonstrate evidence suggesting that redox regulation of NF kappa B by Trx might be exerted at a step after dissociation of the inhibitory molecule I kappa B, a cytosolic-anchoring protein for NF kappa B. To examine the effect of Trx in intact cells, we performed transient assay with a chloramphenicol acetyltransferase-expressing plasmid under the control of human immunodeficiency virus (HIV) long terminal repeat and an effector plasmid expressing human Trx. The promoter activity from HIV long terminal repeat was greatly augmented by co-transfecting the Trx-expressing plasmid, whose effect was dependent on the NF kappa B-binding sites. These findings have suggested that cysteine residue(s) of NF kappa B might be involved in the DNA-recognition by NF kappa B and that the redox control mechanism mediated by Trx might have a regulatory role in the NF kappa B-mediated gene expression. These results may also provide a clue to understanding of the molecular process of AIDS pathogenesis and its possible biochemical intervention.

Tags: Comparative Study; Human; Support, Non-U.S. Gov't
Descriptors: Lymphocytes--metabolism--ME; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --metabolism--ME; Amino Acid Sequence; Animals; Base Sequence ; Binding Sites; Cell Line; Cell Nucleus--metabolism--ME; Cells, Cultured; Cytosol--metabolism--ME; Enhancer Elements (Genetics); Gene Expression; HIV Long Terminal Repeat; HIV-1--genetics--GE; Kinetics; Molecular Sequence Data; **NF-kappa B** --genetics--GE; **NF-kappa B** --isolation and purification --IP; Nuclear Proteins--isolation and purification--IP; Nuclear Proteins --metabolism--ME; Oligodeoxyribonucleotides--chemical synthesis--CS; Oligodeoxyribonucleotides--metabolism--ME; Oxidation-Reduction; Receptors, Interleukin-2--genetics--GE; Sequence Homology, Amino Acid; Time Factors; Transfection
CAS Registry No.: 0 (NF-kappa B); 0 (Nuclear Proteins); 0 (Oligodeoxyribonucleotides); 0 (Receptors, Interleukin-2); 52500-60-4 (Thioredoxin)
Record Date Created: 19930624
Record Date Completed: 19930624

13/9/41
DIALOG(R)File 155:MEDLINE(R)

09703564 PMID: 8491191
H2O2 and antioxidants have opposite effects on activation of NF-kappa B and AP-1 in intact cells: AP-1 as secondary antioxidant-responsive factor.
Meyer M; Schreck R; Baeuerle P A
Laboratory for Molecular Biology of the Ludwig-Maximilians-University, Martinsried, Germany.
EMBO journal (ENGLAND) May 1993, 12 (5) p2005-15, ISSN 0261-4189 Journal Code: 8208664
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Subfile: INDEX MEDICUS

We show that AP-1 is an antioxidant-responsive transcription factor. DNA binding and transactivation by AP-1 were induced in HeLa cells upon treatment with the antioxidants pyrrolidine dithiocarbamate (PDTC) and N-acetyl-L-cysteine (NAC), and upon transient expression of the antioxidative enzyme **thioredoxin** . While PDTC and NAC enhanced DNA binding and transactivation of AP-1 in response to phorbol ester, the oxidant H2O2 suppressed phorbol ester activation of the factor. H2O2 on its own was only a weak inducer of AP-1. Activation of AP-1 by PDTC was dependent on protein synthesis and involved transcriptional induction of c-jun and c-fos genes. Transcriptional activation of c-fos by PDTC was conferred by the serum response element, suggesting that serum response factor and associated proteins function as primary antioxidant-responsive transcription factors. In the same cell line, the oxidative stress-responsive transcription factor NF-kappa B behaved in a manner strikingly opposite to AP-1. DNA binding and transactivation by NF-kappa B were strongly activated by H2O2, while the antioxidants alone were ineffective. H2O2 potentiated the activation of NF-kappa B by phorbol ester, while PDTC and NAC suppressed PMA activation of the factor. PDTC did not influence protein kinase C (PKC) activity and PKC activation by PMA, indicating that the antioxidant acted downstream of and independently from PKC.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Antioxidants--pharmacology--PD; *Hydrogen Peroxide --pharmacology--PD; * **NF-kappa B** --metabolism--ME; *Proto-Oncogene Proteins c-jun--metabolism--ME; Base Sequence; DNA; Genes, fos; Genes, jun; Hela Cells; Molecular Sequence Data; Oligodeoxyribonucleotides; Pyrrolidines --pharmacology--PD; Regulatory Sequences, Nucleic Acid; Tetradecanoylphorbol Acetate--pharmacology--PD; Thiocarbamates--pharmacology--PD; **Thioredoxin** --biosynthesis--BI; Trans-Activation (Genetics); Transcription, Genetic

CAS Registry No.: 0 (Antioxidants); 0 (NF-kappa B); 0 (Oligodeoxyribonucleotides); 0 (Proto-Oncogene Proteins c-jun); 0 (Pyrrolidines); 0 (Thiocarbamates); 16561-29-8 (Tetradecanoylphorbol Acetate); 25769-03-3 (pyrrolidine dithiocarbamic acid); 52500-60-4 (Thioredoxin); 7722-84-1 (Hydrogen Peroxide); 9007-49-2 (DNA)

Gene Symbol: c-fos; c-jun

Record Date Created: 19930611

Record Date Completed: 19930611

13/9/42

DIALOG(R)File 155:MEDLINE(R)

09412140 PMID: 1508666

Thioredoxin **regulates the DNA binding activity of NF-kappa B by reduction of a disulphide bond involving cysteine 62.**

Matthews J R; Wakasugi N; Virelizier J L; Yodoi J; Hay R T

Division of Biochemistry and Molecular Biology, School of Biological and Medical Sciences, University of St Andrews, Fife, UK.

Nucleic acids research (ENGLAND) Aug 11 1992, 20 (15) p3821-30, ISSN 0305-1048 Journal Code: 0411011

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

A role for redox regulation in activation of the NF-kappa B transcription factor was suggested by the observation that DNA binding activity of free protein, but not preformed DNA-protein complex, is inhibited by -SH modifying agents but enhanced by reducing agents. Mutagenesis of conserved cysteine residues in the p50 subunit identified amino acid 62 as being important for DNA binding, as a serine substitution at this position reduces DNA binding affinity, but renders the protein insensitive to -SH modifying agents. DNA binding activity of the wild type protein but not the amino acid 62 mutant was also stimulated by **thioredoxin** while detection of disulphide cross linked dimers in p50 but not the amino acid 62 mutant suggests that **thioredoxin** stimulates DNA binding by reduction of a

disulphide bond involving cysteine 62. The physiological relevance of these findings was supported by the observation that cotransfection of a plasmid expressing human **thioredoxin** and an HIV LTR driven reporter construct resulted in an NF-kappa B dependent increase in expression of the reporter gene. Thus modification of p50 by **thioredoxin** , a gene induced by stimulation of T-lymphocytes in parallel with NF-kappa B translocation, is a likely step in the cascade of events leading to full NF-kappa B activation.

Tags: Support, Non-U.S. Gov't

Descriptors: Cysteine--metabolism--ME; *DNA--metabolism--ME; *Disulfides --metabolism--ME; * **NF-kappa B** --metabolism--ME; * **Thioredoxin** --metabolism --ME; Amino Acid Sequence; Base Sequence; Cell Line; Cloning, Molecular; HIV Long Terminal Repeat--genetics--GE; HIV-1--genetics--GE; Molecular Sequence Data; Oxidation-Reduction; Plasmids--genetics--GE; T-Lymphocytes; Transcription, Genetic--genetics--GE

CAS Registry No.: 0 (Disulfides); 0 (NF-kappa B); 0 (Plasmids); 52-90-4 (Cysteine); 52500-60-4 (Thioredoxin); 9007-49-2 (DNA)

Record Date Created: 19920923

Record Date Completed: 19920923

13/9/43

09397071 PMID: 1498089

Human thioredoxin **/adult T cell leukemia-derived factor activates the enhancer binding protein of human immunodeficiency virus type 1 by thiol redox control mechanism.**

Okamoto T; Ogiwara H; Hayashi T; Mitsui A; Kawabe T; Yodoi J

Virology Division, National Cancer Center Research Institute, Tokyo, Japan.

International immunology (ENGLAND) Jul 1992, 4 (7) p811-9, ISSN 0953-8178 Journal Code: 8916182

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS; AIDS/HIV

Transcription from the human immunodeficiency virus type 1 (HIV-1) provirus is activated by a cellular factor, NF kappa B, recognizing the tandemly repeated 10-base-pair sequences, termed the kappa B sequence, present in the enhancer region within the viral long terminal repeat (LTR). Using electrophoretic mobility shift assay (EMSA), which demonstrates specific DNA-protein interaction in vitro, we could demonstrate that reducto-oxidative modulation of NF kappa B dramatically changes its DNA binding activity and that a cellular physiological reducing catalyst, **thioredoxin** (TRX) also known as adult T cell leukemia derived factor (ADF), fully restored the DNA-binding activity of the oxidized NF kappa B. We also observed that purified TRX/ADF protein could augment gene expression from HIV LTR as demonstrated by transient chloramphenicol acetyltransferase (CAT) assay. These observations confirmed the previous notion that ADF might be an inducing factor of cellular interleukin-2 receptor alpha subunit (IL-2R alpha) through the kappa B sequence that is a common central cis-regulatory element in both IL-2R alpha and HIV gene expression. These observations indicate that reducto-oxidative regulation (or redox regulation) of a cysteine residue(s) on the NF kappa B molecule might play an important role in its specific DNA interaction and that it might provide a clue to the understanding of a pathway of cellular signal transduction to NF kappa B that is independent from the known pathways involving protein phosphorylation.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: Cytokines; * **HIV Enhancer** --drug effects--DE; *HIV-1--drug effects--DE; *HIV-1--metabolism--ME; *Neoplasm Proteins--pharmacology--PD; * **Thioredoxin** --pharmacology--PD; Amino Acid Sequence; Base Sequence; Binding Sites; DNA, Viral--genetics--GE; DNA, Viral--metabolism--ME; Gene Expression--drug effects--DE; **HIV Enhancer** --physiology--PH; HIV-1

--genetics--GE; Molecular Sequence Data; **NF-kappa B** --genetics--GE; **NF-kappa B** --metabolism--ME; Oxidation-Reduction; Signal Transduction; Sulfhydryl Compounds--metabolism--ME
CAS Registry No.: 0 (Cytokines); 0 (DNA, Viral); 0 (NF-kappa B); 0 (Neoplasm Proteins); 0 (Sulfhydryl Compounds); 0 (adult T cell leukemia-derived factor); 52500-60-4 (Thioredoxin)
Record Date Created: 19920911
Record Date Completed: 19920911
?ds

Set	Items	Description
S1	1	'NF KAPPA B'
S2	0	E6 OR E5
S3	12838	E4-E36
S4	13161	R1-R10
S5	5	'THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD'
S6	37	'THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI'
S7	201	'THIOREDOXIN --PHARMACOLOGY --PD'
S8	8	'THIOREDOXIN --THERAPEUTIC USE --TU'
S9	3248	E3-E32
S10	3248	'THIOREDOXIN' OR DC='D12.776.915.'
S11	54	(S1 OR S2 OR S3 OR S4) AND (S5 OR S6 OR S7 OR S8 OR S9 OR S10)
S12	11	S11/2002:2004
S13	43	S11 NOT S12

?e cgpc

Ref	Items	Index-term
E1	1	CGPAHS
E2	1	CGPASE
E3	12	*CGPC
E4	1	CGPCSD
E5	7	CGPD
E6	1	CGPDE
E7	5	CGPDH
E8	1	CGPDS
E9	2	CGPE
E10	2	CGPEI
E11	1	CGPEMLNRVSEPGC
E12	1	CGPGC

Enter P or PAGE for more
?s e3
S14 12 'CGPC'
?t s14/9/all

14/9/1
DIALOG(R)File 155:MEDLINE(R)

15877813 PMID: 12832786
Purification, crystallization and preliminary X-ray analysis of an unusual thioredoxin from the gastric pathogen Helicobacter pylori.
Filson Heather; Fox Aine; Kelleher Dermot; Windle Henry J; Sanders David A R
Department of Chemistry, University of Saskatchewan, Saskatoon, Saskatchewan S7N 5C9, Canada.
Acta crystallographica. Section D, Biological crystallography (Denmark) Jul 2003, 59 (Pt 7) p1280-2, ISSN 0907-4449 Journal Code: 9305878
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Thioredoxin-2 (HP1458) from Helicobacter pylori is a member of the thioredoxin family, but possesses the unusual active-site motif CPDC (compared with **CGPC** in other thioredoxins). H. pylori is deficient in the

glutaredoxin system, making the thioredoxin system the sole reduction system in the bacterium and critical for its ability to survive oxidative stress. The recombinant protein has been overexpressed, purified and crystallized. This is the first reported crystallization of a thioredoxin possessing this unusual active site. Single crystals have been obtained using the sitting-drop technique. Crystals diffract to 2.4 A resolution and belong to space group P4(1), with unit-cell parameters a = b = 40.21, c = 64.65 A. Molecular replacement using AMoRe proved unsuccessful; however, implementation of the program BEAST gave successful molecular-replacement solutions.

Tags: Support, Non-U.S. Gov't

Descriptors: *Helicobacter pylori--chemistry--CH; *Thioredoxin--chemistry --CH; Amino Acid Motifs; Binding Sites; Crystallization--methods--MT; Recombinant Proteins; Thioredoxin--genetics--GE; Thioredoxin--isolation and purification--IP; X-Ray Diffraction--methods--MT

CAS Registry No.: 0 (Recombinant Proteins); 52500-60-4 (Thioredoxin)

Record Date Created: 20030630

Record Date Completed: 20040325

14/9/2

DIALOG(R)File 155:MEDLINE(R)

13981946 PMID: 9680968

A novel thioredoxin-like protein located in the chloroplast is induced by water deficit in Solanum tuberosum L. plants.

Rey P; Pruvot G; Becuwe N; Eymery F; Rumeau D; Peltier G

CEA/Cadarache, DSV, DEVM, Departement d'Ecophysiologie Vegetale et de Microbiologie, Batiment 161, Saint-Paul-lez-Durance, France. Rey@dsvcad.cea.fr

Plant journal - for cell and molecular biology (ENGLAND) Jan 1998, 13 (1) p97-107, ISSN 0960-7412 Journal Code: 9207397

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

By analysing two-dimensional patterns of chloroplastic proteins from Solanum tuberosum, the authors observed the accumulation of a 32-kDa polypeptide in the stroma of plants subjected to water deficit. N-terminus and internal peptides of the protein, named CDSP 32 for chloroplastic drought-induced stress protein, showed no obvious homology with known sequences. Using a serum raised against the protein N-terminus, a cDNA encoding CDSP 32 was cloned by screening an expression library. The deduced mature CDSP 32 protein is 243 amino acids long and displays typical features of thioredoxins in the C-terminal region (122 residues). In particular, CDSP 32 contains a **CGPC** motif corresponding to a thioredoxin active site and a number of amino acids conferring thioredoxin-type structure. The CDSP 32 C-terminal region was expressed as a fusion protein in Escherichia coli and was shown to possess thioredoxin activity based on reduction assay of insulin disulfide bridges. RNA blot analysis showed that CDSP 32 transcript does not accumulate upon mild water deficit conditions corresponding to leaf relative water contents (RWC) around 85%, but high levels of CDSP 32 transcripts were observed for more severe stress conditions (RWC around 70%). In vivo labelling and immunoprecipitation revealed a substantial increase in CDSP 32 synthesis upon similar stress conditions. Rewatering of wilted plants caused decreases in both transcript and protein abundances. In tomato wild-type plants and ABA-deficient mutants, a similar accumulation of a CDSP 32-related transcript was observed upon water deficit, most likely indicating no requirement for ABA in the regulation of CDSP 32 synthesis. Based on these results, it is proposed that CDSP 32 plays a role in preservation of the thiol: disulfide redox potential of chloroplastic proteins during water deficit.

Descriptors: *Plant Proteins--biosynthesis--BI; *Potatoes--metabolism--ME ; *Thioredoxin--biosynthesis--BI; Amino Acid Sequence; Base Sequence; Chloroplasts--metabolism--ME; Cloning, Molecular; DNA, Complementary

--genetics--GE; DNA, Plant--genetics--GE; Escherichia coli--genetics--GE; Gene Expression Regulation, Plant; Genes, Plant; Molecular Sequence Data; Molecular Weight; Plant Proteins--genetics--GE; Plant Proteins--isolation and purification--IP; Potatoes--genetics--GE; Recombinant Proteins --genetics--GE; Recombinant Proteins--isolation and purification--IP; Sequence Homology, Amino Acid; Solubility; Thioredoxin--genetics--GE; Thioredoxin--isolation and purification--IP; Water--metabolism--ME
Molecular Sequence Databank No.: GENBANK/Y09987
CAS Registry No.: 0 (DNA, Complementary); 0 (DNA, Plant); 0 (Plant Proteins); 0 (Recombinant Proteins); 0 (thioredoxin-like protein); 52500-60-4 (Thioredoxin); 7732-18-5 (Water)
Record Date Created: 19980820
Record Date Completed: 19980820

14/9/3
DIALOG(R)File 155:MEDLINE(R)

13782096 PMID: 9473519
Molecular cloning and expression of a cDNA encoding a human thioredoxin-like protein.
Miranda-Vizuete A; Gustafsson J A; Spyrou G
Department of Biosciences at Novum, Karolinska Institute, Huddinge, Sweden.
Biochemical and biophysical research communications (UNITED STATES) Feb 4 1998, 243 (1) p284-8, ISSN 0006-291X Journal Code: 0372516
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
This report describes the cloning of a human cDNA that encodes a new protein (Txl, Thioredoxin-like) that belongs to the expanding family of thioredoxins based on sequence comparison of the deduced amino acid sequence. This cDNA, with a total length of 1,278 bp, consists of 205 bp of 5'-untranslated sequence (including an in frame stop codon), an open reading frame of 870 bp and a 203 bp fragment of 3'-untranslated sequence. The coding sequence predicts a protein of 289 amino acids with two distinct domains: an N-terminal domain of 105 residues homologous to the rest of mammalian thioredoxins containing the conserved active site (**CGPC**) and a C-terminal domain of 184 residues with no homology with any other protein in the database. Northern blot analysis indicates that the txl probe hybridizes to a 1.3 Kb mRNA and is ubiquitously expressed in human tissues with the highest expression in stomach, testis and bone marrow.
Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't
Descriptors: *DNA, Complementary--genetics--GE; *Thioredoxin--genetics --GE; Amino Acid Sequence; Animals; Base Sequence; Binding Sites--genetics --GE; Cloning, Molecular; DNA Primers--genetics--GE; Gene Expression; Membrane Proteins--chemistry--CH; Membrane Proteins--genetics--GE; Molecular Sequence Data; Polymerase Chain Reaction; RNA, Messenger --genetics--GE; RNA, Messenger--metabolism--ME; Rats; Sequence Homology, Amino Acid; Thioredoxin--chemistry--CH; Tissue Distribution
Molecular Sequence Databank No.: GENBANK/AF003938
CAS Registry No.: 0 (DNA Primers); 0 (DNA, Complementary); 0 (Membrane Proteins); 0 (RNA, Messenger); 0 (TRX1 protein); 0 (TRX2 protein); 0 (thioredoxin-like protein); 52500-60-4 (Thioredoxin)
Record Date Created: 19980316
Record Date Completed: 19980316

14/9/4
DIALOG(R)File 155:MEDLINE(R)

13711115 PMID: 9398223
Microscopic pKa values of Escherichia coli thioredoxin.

Chivers P T; Prehoda K E; Volkman B F; Kim B M; Markley J L; Raines R T
Department of Biochemistry, University of Wisconsin-Madison 53706, USA.
Biochemistry (UNITED STATES) Dec 2 1997, 36 (48) p14985-91, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: GM08293; GM; NIGMS; GM35976; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Thiol:disulfide oxidoreductases have a CXXC motif within their active sites. To initiate the reduction of a substrate disulfide bond, the thiolate form of the N-terminal cysteine residue (CXXC) of this motif performs a nucleophilic attack. Escherichia coli thioredoxin [Trx (**CGPC**)] is the best characterized thiol:disulfide oxidoreductase. Previous determinations of the active-site pKa values of Trx have led to conflicting interpretations. Here, 13C-NMR spectroscopy, site-specific isotopic labeling, and site-directed mutagenesis were used to demonstrate that analysis of the titration behavior of wild-type Trx requires the invocation of microscopic pKa values for two interacting active-site residues: Asp26 (7.5 and 9.2) and Cys32 (CXXC; 7.5 and 9.2). By contrast, in two Trx variants, D26N Trx and D26L Trx, Cys32 exhibits a pKa near 7.5 and has a well-defined, single-pKa titration curve. Similarly, in oxidized wild-type Trx, Asp26 has a pKa near 7.5. In CVWC and CWGC Trx, Cys32 exhibits a single pKa near 6.2. In all five enzymes studied here, there is no evidence for a Cys35 (CXXC) pKa of < 11. This study demonstrates that a comprehensive approach must be used to unravel complex titration behavior of the functional groups in a protein.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: *Escherichia coli--enzymology--EN; *Protein Disulfide Reductase (Glutathione)--chemistry--CH; *Thioredoxin--chemistry--CH; Acids --chemistry--CH; Binding Sites; Carbon Isotopes; Hydrogen-Ion Concentration ; Models, Chemical; Mutagenesis, Site-Directed; Nuclear Magnetic Resonance, Biomolecular; Protein Disulfide Reductase (Glutathione)--genetics--GE; Recombinant Proteins--chemistry--CH; Statistics; Thioredoxin--genetics--GE; Titrimetry; Variation (Genetics)
CAS Registry No.: 0 (Acids); 0 (Carbon Isotopes); 0 (Recombinant Proteins); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 1.8.4.2 (Protein Disulfide Reductase (Glutathione))
Record Date Created: 19980108
Record Date Completed: 19980108

14/9/5
DIALOG(R)File 155:MEDLINE(R)

13427308 PMID: 9099998
The CXXC motif: a rheostat in the active site.
Chivers P T; Prehoda K E; Raines R T
Department of Biochemistry, University of Wisconsin-Madison, 53706, USA.
Biochemistry (UNITED STATES) Apr 8 1997, 36 (14) p4061-6, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: GM08293; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The active-site CXXC motif of thiol:disulfide oxidoreductases is essential for their catalysis of redox reactions. Changing the XX residues can perturb the reduction potential of the active-site disulfide bond of the Escherichia coli enzymes thioredoxin (Trx; **CGPC**) and DsbA (CPHC). The reduction potential is correlated with the acidity of the N-terminal cysteine residue of the CXXC motif. As the pKa is lowered, the disulfide bond becomes more easy to reduce. A change in pKa can account fully for a

change in reduction potential in well-characterized CXXC motifs of DsbA but not of Trx. Formal analysis of the Nernst equation reveals that reduction potential contains both pH-dependent and pH-independent components. Indeed, the difference between the reduction potentials of wild-type Trx and wild-type DsbA cannot be explained solely by differences in thiol pKa values. Structural data for thiol:disulfide oxidoreductases reveal no single factor that determines the pH-independent component of the reduction potential. In addition, the pH-dependent component is complex when the redox state of the CXXC motif affects the titration of residues other than the thiols. These intricacies enable CXXC motifs to vary widely in their capacity to assist electron flow, and thereby engender a family of thiol:disulfide oxidoreductases that play diverse roles in biochemistry.

Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *Escherichia coli--enzymology--EN; *Protein Disulfide Reductase (Glutathione)--chemistry--CH; Binding Sites; Crystallography, X-Ray; Cysteine--chemistry--CH; Disulfides--chemistry--CH; Electrochemistry ; Electron Transport; Glutathione--metabolism--ME; Hydrogen-Ion Concentration; Molecular Sequence Data; Oxidation-Reduction; Protein Disulfide Reductase (Glutathione)--metabolism--ME; Sulfhydryl Compounds --chemistry--CH

Molecular Sequence Databank No.: PDB/1AAZ; PDB/1ABA; PDB/1DSB; PDB/1THX; PDB/1XOA; PDB/2TRX

CAS Registry No.: 0 (Disulfides); 0 (Sulfhydryl Compounds); 52-90-4 (Cysteine); 70-18-8 (Glutathione)

Enzyme No.: EC 1.8.4.2 (Protein Disulfide Reductase (Glutathione))

Record Date Created: 19970515

Record Date Completed: 19970515

14/9/6

DIALOG(R)File 155:MEDLINE(R)

12429627 PMID: 12743836

Long-term clinical performance and longevity of gold alloy vs ceramic partial crowns.

Wagner J; Hiller K-A; Schmalz G

Dental School, University of Regensburg, Regensburg, Germany.

Clinical oral investigations (Germany) Jun 2003, 7 (2) p80-5, ISSN 1432-6981 Journal Code: 9707115

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: DENTAL

Cast gold partial crowns (**CGPC**) are an accepted means of restoring posterior teeth. For aesthetic reasons, gold alloys are being increasingly substituted with ceramics. The aim of the present study was to investigate retrospectively the long-term clinical performance and survival of **CGPC** and compare the results to the ones already reported for ceramic partial crowns (CPC). The **CGPC** group consisted of 42 patients (24 male, 18 female) randomly sampled from a total of 106 patients with **CGPC** , with one restoration per patient. The CPC group consisted of 22 patients with a total of 42 restorations. Both types of restoration were done by one experienced dentist. Another two experienced dentists who were not involved in performing the restorations rated both kinds of partial crowns using the modified United State Public Health Service (USPHS) criteria [14]. The Median age of the **CGPC** was 57 months (range 3-157) and of the CPC and 63 months (range 24-72). Forty-one (98%) of the **CGPC** and 27 (64%) of the CPC were placed in molars, the rest in premolars. In each group, 40 (95%) restorations were still functioning without any necessity of replacement. Two teeth with **CGPC** , in situ for 4.5 and 11 years, respectively, had been extracted for periodontal reasons. Two CPC fractured and had to be replaced after 2 and 6.5 years in situ. The USPHS criteria results were similarly good for the gold and ceramic groups. Kaplan-Meier analysis revealed

survival probabilities of 72+/-21% and 96+/-4% after 13 and 7 years, respectively, for the **CGPC** . Survival of the CPC was 81+/-15% after 7 years. No statistically significant difference among survival functions of **CGPC** and CPC was found. From this data, it can be concluded that the longevity of CPC is not inferior to that of gold alloys. However, more long-term studies comparing the clinical performance and longevity of these two types of indirect restoration in the posterior region with larger numbers of restorations are desirable.

Tags: Comparative Study; Female; Human; Male

Descriptors: *Ceramics; *Crowns; *Dental Prosthesis Design; *Gold Alloys ; Bicuspid; Ceramics--chemistry--CH; Crowns--statistics and numerical data --SN; Dental Bonding; Dental Caries--classification--CL; Dental Restoration Failure; Dentin Sensitivity--classification--CL; Follow-Up Studies; Gold Alloys--chemistry--CH; Molar; Retrospective Studies; Surface Properties; Survival Analysis; Time Factors

CAS Registry No.: 0 (Ceramics); 0 (Gold Alloys)

Record Date Created: 20030701

Record Date Completed: 20031027

Date of Electronic Publication: 20030513

14/9/7

DIALOG(R)File 155:MEDLINE(R)

12358447 PMID: 12731880

The CXC motif: a functional mimic of protein disulfide isomerase.

Woycechowsky Kenneth J; Raines Ronald T

Department of Biochemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA.

Biochemistry (United States) May 13 2003, 42 (18) p5387-94, ISSN 0006-2960 Journal Code: 0370623

Contract/Grant No.: GM08505; GM; NIGMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Protein disulfide isomerase (PDI) utilizes the active site sequence Cys-Gly-His-Cys (CGHC; E degrees ' = -180 mV) to effect thiol-disulfide interchange during oxidative protein folding. Here, the Cys-Gly-Cys-NH(2) (CGC) peptide is shown to have a disulfide reduction potential (E degrees ' = -167 mV) that is close to that of PDI. This peptide has a thiol acid dissociation constant (pK(a) = 8.7) that is lower than that of glutathione. These attributes endow the CGC peptide with substantial disulfide isomerization activity. Escherichia coli thioredoxin (Trx) utilizes the active site sequence Cys-Gly-Pro-Cys (**CGPC** ; E degrees ' = -270 mV) to effect disulfide reduction. Removal of the proline residue from the Trx active site yields a CGC active site with a greatly destabilized disulfide bond (E degrees ' >or= -200 mV). The DeltaP34 variant retains high conformational stability and remains a substrate for thioredoxin reductase. In contrast to the reduced form of the wild-type enzyme, the reduced form of DeltaP34 Trx has disulfide isomerization activity, which is 25-fold greater than that of the CGC peptide. Thus, the rational deletion of an active site residue can bestow a new and desirable function upon an enzyme. Moreover, a CXC motif, in both a peptide and a protein, provides functional mimicry of PDI.

Tags: Comparative Study; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.

Descriptors: *Escherichia coli--enzymology--EN; *Escherichia coli --metabolism--ME; *Molecular Mimicry; *Protein Disulfide-Isomerase --metabolism--ME; *Thioredoxin--metabolism--ME; Amino Acid Motifs; Binding Sites; Cysteine--chemistry--CH; Disulfides--chemistry--CH; Disulfides --metabolism--ME; Genetic Vectors; Kinetics; Mutation; NADP--metabolism--ME ; Oxidation-Reduction; Protein Conformation; Protein Disulfide-Isomerase --chemistry--CH; Protein Folding; Spectrometry, Fluorescence; Substrate Specificity; Sulfhydryl Compounds--chemistry--CH; Sulfhydryl Compounds

--metabolism--ME; Thioredoxin--genetics--GE; Thioredoxin Reductase (NADPH) --metabolism--ME
CAS Registry No.: 0 (Disulfides); 0 (Genetic Vectors); 0 (Sulfhydryl Compounds); 52-90-4 (Cysteine); 52500-60-4 (Thioredoxin); 53-59-8 (NADP)
Enzyme No.: EC 1.6.4.5 (Thioredoxin Reductase (NADPH)); EC 5.3.4.1 (Protein Disulfide-Isomerase)
Record Date Created: 20030506
Record Date Completed: 20030624

14/9/8
DIALOG(R)File 155:MEDLINE(R)

11817034 PMID: 11867629
Catalytic properties, thiol pK value, and redox potential of Trypanosoma brucei tryparedoxin.
Reckenfelderbaumer Nina; Krauth-Siegel R Luise
Biochemie-Zentrum Heidelberg, Universitat Heidelberg, 69120 Heidelberg, Germany.
Journal of biological chemistry (United States) May 17 2002, 277 (20) p17548-55, ISSN 0021-9258 Journal Code: 2985121R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The dithiol protein tryparedoxin is a component of the unique trypanothione/trypanothione reductase metabolism of trypanosomatids and is involved in the parasite synthesis of deoxyribonucleotides and the detoxication of hydroperoxides. Tryparedoxin is a highly abundant protein in all life stages of Trypanosoma brucei, the causative agent of African sleeping sickness. As shown here, its functional properties are intermediate between those of classical thioredoxins and glutaredoxins. The redox potential of T. brucei tryparedoxin of -249 mV was determined by protein-protein redox equilibration with Escherichia coli thioredoxin. The trypanothione/tryparedoxin couple is probably the most significant factor determining the cytosolic redox potential of the parasites. The pK value of Cys(40), the first thiol in the WCPPC motif, is 7.2 as derived from the thiolate absorption at 240 nm and the rate of carboxymethylation. Alteration of the active site into that of thioredoxin (**CGPC**) did not affect the pK value. In contrast, in the mutant with the glutaredoxin motif (CPYC) the pK dropped to < or =4.0. The fact that the pK value of tryparedoxin coincides with the intracellular pH of the parasite may contribute to the reactivity of tryparedoxin in thiol disulfide exchange reactions.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *Sulfhydryl Compounds--metabolism--ME; *Thioredoxin --metabolism--ME; *Trypanosoma brucei brucei--metabolism--ME; Alkylation; Amino Acid Substitution; Animals; Catalysis; Chromatography, High Pressure Liquid; Dehydroascorbic Acid--metabolism--ME; Enzyme Activation; Hydrogen-Ion Concentration; Kinetics; Malate Dehydrogenase--metabolism--ME; Mutagenesis, Site-Directed; Oxidation-Reduction; Spectrophotometry, Atomic; Thioredoxin--genetics--GE; Thioredoxin Reductase (NADPH)--metabolism--ME
CAS Registry No.: 0 (Sulfhydryl Compounds); 0 (tryparedoxin); 490-83-5 (Dehydroascorbic Acid); 52500-60-4 (Thioredoxin)
Enzyme No.: EC 1.1.1.37 (Malate Dehydrogenase); EC 1.6.4.5 (Thioredoxin Reductase (NADPH))
Record Date Created: 20020513
Record Date Completed: 20020716
Date of Electronic Publication: 20020226

14/9/9
DIALOG(R)File 155:MEDLINE(R)

Stimulated by a number of general practitioners and with the support of the Canadian Medical Association, the College of General Practitioners of Canada (**CGPC**) was founded in 1954. In 1962, conferences on education for general practice attended by the Association of Canadian Medical Colleges and the **CGPC** led to pilot postgraduate residencies in family practice supported by Department of National Health and Welfare. The first certification examination was held in 1969 and, by 1974, all Canadian medical schools had a family medicine residency program. Today departments of family medicine contribute substantially to undergraduate education in all 16 schools. In Canada, the medical profession, governments and the medical schools have demonstrated the importance they place on appropriate education for family physicians.

Descriptors: *Family Practice--trends--TD; Canada; Certification; Family Practice--education--ED; Internship and Residency

Record Date Created: 19930527

Record Date Completed: 19930527

14/9/12

DIALOG(R)File 155:MEDLINE(R)

08448979 PMID: 1689759

Differential expression of type I hair keratins.

Bertolino A P; Checkla D M; Heitner S; Freedberg I M; Yu D W

Department of Dermatology, New York University Medical Center, New York.

Journal of investigative dermatology (UNITED STATES) Mar 1990, 94 (3) p297-303, ISSN 0022-202X Journal Code: 0426720

Contract/Grant No.: 1F32 AM06507-01; AM; NIADDK; 1R23 AR35644-01; AR; NIAMS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The hair follicle provides an excellent system in which to study growth and differentiation. Hair keratins are useful tissue-specific molecular markers for these events. By comparing a second mouse Type I hair keratin cDNA clone, MHKA-2, with our previously described MHKA-1, we have been able to contrast the nucleotide sequences and corresponding deduced amino acid sequences of the smallest (mHa4) and the largest (mHa1) major Type I hair keratins. Both nucleotide sequences and both deduced amino acid sequences share high identity but have distinct segments suitable for generation of specific molecular probes. Comparison of amino acid sequences adjacent to the central helical domains has demonstrated homologous subdomains, designated H1 and H2, in the Type I hair keratin nonhelical termini. Although there is only 56% amino acid identity in the carboxy-terminal nonhelical domains, a common sequence, T------- **CGPC** ----R, has been identified in this domain, suggesting a possible common functional role for this portion of the molecule. In addition, it appears that mHa4 may differ in part from mHa1 by deletion of a segment between the H2 subdomain and the conserved sequence. Staining of mouse and human hair follicles with AmHa1, a monospecific polyclonal antibody for mHa1, and AE13, an antibody specific for all Type I hair keratins, suggests differential expression of individual Type I hair keratins in both species. This supports our hypothesis that distinct functional requirements are satisfied by the multiplicity of hair keratins.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Hair--metabolism--ME; *Keratin--genetics--GE; Amino Acid Sequence; Animals; Antibodies--immunology--IM; Antibody Specificity; Base Sequence; Cloning, Molecular; DNA--genetics--GE; Keratin--immunology--IM; Keratin--metabolism--ME; Mice; Molecular Sequence Data; Tissue Distribution

CAS Registry No.: 0 (Antibodies); 68238-35-7 (Keratin); 9007-49-2 (DNA)

Record Date Created: 19900402

Record Date Completed: 19900402

?ds

Set	Items	Description
S1	1	'NF KAPPA B'
S2	0	E6 OR E5
S3	12838	E4-E36
S4	13161	R1-R10
S5	5	'THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD'
S6	37	'THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI'
S7	201	'THIOREDOXIN --PHARMACOLOGY --PD'
S8	8	'THIOREDOXIN --THERAPEUTIC USE --TU'
S9	3248	E3-E32
S10	3248	'THIOREDOXIN' OR DC='D12.776.915.'
S11	54	(S1 OR S2 OR S3 OR S4) AND (S5 OR S6 OR S7 OR S8 OR S9 OR S10)
S12	11	S11/2002:2004
S13	43	S11 NOT S12
S14	12	'CGPC'

?t s5/9/all

5/9/1

DIALOG(R)File 155:MEDLINE(R)

13576702 PMID: 9264384

Interleukin-15 + thioredoxin induce DNA synthesis in B-chronic lymphocytic leukemia cells but not in normal B cells.

Soderberg O; Christiansen I; Nilsson G; Carlsson M; Nilsson K
Department of Pathology, University of Uppsala, University Hospital, Sweden.

Leukemia - official journal of the Leukemia Society of America, Leukemia Research Fund, U.K (ENGLAND) Aug 1997, 11 (8) p1298-304, ISSN 0887-6924 Journal Code: 8704895
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

We have previously shown that Staphylococcus aureus Cowan strain 1 particles (SAC) + thioredoxin (Trx) + IL-2 may induce B-chronic lymphocytic leukemia (B-CLL) cells to proliferate. In this paper we have examined IL-15, which has activities similar to IL-2, for its ability to stimulate B-CLL cells and compared its activity with that of IL-2. We found that B-CLL cells could be induced to DNA synthesis upon treatment with IL-15 + Trx. The presence of Trx was essential for the IL-15-induced DNA synthesis. This contrasts to the effect of IL-15 + Trx on normal CD5+ and CD5- B cells, where IL-15 + Trx alone only induced limited DNA synthesis. IL-15 was as effective in the induction of DNA synthesis in B-CLL cells as IL-2, but about 100-fold less potent with an EC50 of 200 ng/ml. In addition we found that the IL-15 + Trx-induced proliferation was inhibited by CD40 stimulation. We conclude that IL-15 together with a proper costimulus can induce B-CLL cells to proliferate in vitro.

Tags: Human; Support, Non-U.S. Gov't
Descriptors: B-Lymphocytes--cytology--CY; *DNA--biosynthesis--BI; *Interleukin-15--administration and dosage--AD; *Leukemia, B-Cell, Chronic --pathology--PA; * **Thioredoxin** --administration and dosage--AD; Antigens, CD40--physiology--PH; Cell Cycle--drug effects--DE; Cell Differentiation --drug effects--DE; Cell Division--drug effects--DE; Lymphocyte Activation; Receptors, Interleukin-2--metabolism--ME; Tumor Cells, Cultured
CAS Registry No.: 0 (Antigens, CD40); 0 (Interleukin-15); 0 (Receptors, Interleukin-2); 52500-60-4 (Thioredoxin); 9007-49-2 (DNA)
Record Date Created: 19970904
Record Date Completed: 19970904

5/9/2

DIALOG(R)File 155:MEDLINE(R)

12856857 PMID: 8545467

Proline, ascorbic acid, or thioredoxin affect jaundice and mortality in Long Evans cinnamon rats.

Hawkins R L; Mori M; Inoue M; Torii K

Torii Nutrient-stasis Project, Research Development Corporation of Japan, Yokohama, Japan.

Pharmacology, biochemistry, and behavior (UNITED STATES) Nov 1995, 52 (3) p509-15, ISSN 0091-3057 Journal Code: 0367050

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The Long Evans Cinnamon (LEC) rat spontaneously develops fulminant hepatitis, which is usually lethal due to excess copper accumulation in the liver and is considered an animal model of Wilson's disease. LEC rats show a strong appetite for proline solution. Daily oral (p.o.) administration of proline resulted in significant delay of mortality. Feeding a copper-deficient diet greatly delayed the onset of jaundice and mortality and voluntary consumption or p.o. administration of proline further delayed jaundice and prevented mortality. LEC rats also consume ascorbic acid solutions, and p.o. administration of ascorbate also results in a significant delay in the appearance of jaundice and mortality. Combined treatment with ascorbic acid and proline is additive to delay further jaundice and mortality. An endogenous antioxidant protein, thioredoxin, when infused by minipump IP, could also inhibit the incidence of jaundice. These results indicate that antioxidant treatment combined with proline may be of benefit in Wilson's disease and possibly other forms of hepatic dysfunction.

Tags: Male

Descriptors: *Antioxidants--therapeutic use--TU; *Ascorbic Acid --therapeutic use--TU; *Jaundice--drug therapy--DT; *Proline--therapeutic use--TU; *Thioredoxin--therapeutic use--TU; Aging--physiology--PH; Animals; Antioxidants--administration and dosage--AD; Ascorbic Acid--administration and dosage--AD; Copper--deficiency--DF; Diet; Infusion Pumps, Implantable; Jaundice--genetics--GE; Jaundice--mortality--MO; Proline--administration and dosage--AD; Rats; Rats, Inbred Strains; **Thioredoxin** --administration and dosage--AD

CAS Registry No.: 0 (Antioxidants); 147-85-3 (Proline); 50-81-7 (Ascorbic Acid); 52500-60-4 (Thioredoxin); 7440-50-8 (Copper)

Record Date Created: 19960214

Record Date Completed: 19960214

5/9/3

DIALOG(R)File 155:MEDLINE(R)

12327202 PMID: 12690627

[Experimental and clinical aspects of oxidative stress and redox regulation]

Nakamura Hajime

Laboratory of Infection and Prevention, Department of Biological Responses, Institute for Virus Research, Kyoto University, Kyoto 606-8507.

Rinsho byori. The Japanese journal of clinical pathology (Japan) Feb 2003, 51 (2) p109-14, ISSN 0047-1860 Journal Code: 2984781R

Document type: Journal Article; Review; Review, Tutorial ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Although excess amounts of oxidative stress damage proteins and nucleotides, small amounts of oxidative stress transduce intracellular signals for cellular activation, differentiation and proliferation.

Reduction/oxidation(redox) regulation is defined as a biological response to maintain homeostasis against oxidative stress. Thioredoxin, a 12 kD small protein with a redox-active dithiol/disulfide in the conserved active site: -Cys-Gly-Pro-Cys-, is a key molecule for redox regulation as well as glutathione(GSH). Thioredoxin is induced by a variety of oxidative stresses and secreted from cells. Thioredoxin plays crucial roles as a redox-regulator of intracellular signal transduction and as a radical scavenger. Plasma levels of thioredoxin are good biomarkers for oxidative stress. Thioredoxin-transgenic mice are more resistant to cerebral infarction, infection or inflammation and survive longer than control mice. Administration of thioredoxin may have a good potential for anti-aging and anti-stress effects. Redox regulation mechanisms by thioredoxin and other thioredoxin family members will clarify the pathophysiology of oxidative stress-associated disorders. (15 Refs.)

Tags: Human

Descriptors: *Oxidation-Reduction; *Oxidative Stress; *Thioredoxin; Animals; Antioxidants; Biological Markers--blood--BL; Cerebral Infarction --drug therapy--DT; Cerebral Infarction--etiology--ET; Inflammation--drug therapy--DT; Inflammation--etiology--ET; Infusions, Intravenous; Mice; Mice, Transgenic; Oxidative Stress--physiology--PH; Reperfusion Injury --drug therapy--DT; Reperfusion Injury--etiology--ET; **Thioredoxin** --administration and dosage--AD; Thioredoxin--blood--BL; Thioredoxin --genetics--GE

CAS Registry No.: 0 (Antioxidants); 0 (Biological Markers); 52500-60-4 (Thioredoxin)

Record Date Created: 20030414

Record Date Completed: 20030602

5/9/4

DIALOG(R)File 155:MEDLINE(R)

11594094 PMID: 11742067

Circulating thioredoxin suppresses lipopolysaccharide-induced neutrophil chemotaxis.

Nakamura H; Herzenberg L A; Bai J; Araya S; Kondo N; Nishinaka Y; Herzenberg L A; Yodoi J

Department of Biological Responses, Institute for Virus Research, Kyoto University, 53 Shogoin-Kawaharacho, Sakyo, Kyoto 606-8507, Japan. hnakamur@virus.kyoto-u.ac.jp

Proceedings of the National Academy of Sciences of the United States of America (United States) Dec 18 2001, 98 (26) p15143-8, ISSN 0027-8424 Journal Code: 7505876

Contract/Grant No.: CA-42509; CA; NCI; CA-81543; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Thioredoxin (Trx), a redox enzyme with a conserved active site (Cys-32-Gly-Pro-Cys-35), is induced and secreted into circulation in response to inflammation. Studies here demonstrate that elevating Trx levels in circulation either by i.v. injection of recombinant Trx or stimulating Trx release in Trx-transgenic mice dramatically blocks lipopolysaccharide (LPS)-stimulated neutrophil migration in the murine air pouch chemotaxis model. Furthermore, we show that leukocyte recruitment induced by the murine chemokines KC/GROalpha, RANTES (regulated upon activation, normal T cell expressed and secreted), and monocyte chemoattractant protein-1 (MCP-1) is suppressed also in Trx-transgenic mice. Addressing the mechanism responsible for this suppression, we show that circulating Trx blocks (i) the LPS-stimulated in vitro activation of neutrophil p38 mitogen-activated protein kinase, (ii) the normal down-regulation of CD62L on neutrophils migrating into the LPS-stimulated air pouch, and (iii) the in vitro adhesion of LPS-activated neutrophils on endothelial cells. However, as we also show, Trx does not alter the expression of endothelial cell adhesion molecules (intercellular adhesion

molecule-1, vascular cell adhesion molecule-1, CD62P, and CD62E) within 3 h. Collectively, these findings indicate that elevated levels of circulating Trx interfere with chemotaxis by acting directly on neutrophils. We discuss these findings in the context of recent studies reporting beneficial effects of acutely elevated Trx in ischemic injury and negative effects associated with chronically elevated Trx in HIV disease.

Tags: Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Descriptors: *Chemotaxis, Leukocyte--physiology--PH; *Lipopolysaccharides --pharmacology--PD; *Neutrophils--drug effects--DE; *Thioredoxin--blood--BL ; Animals; Cell Adhesion--physiology--PH; Down-Regulation--drug effects--DE ; Enzyme Activation; Mice; Mice, Inbred BALB C; Mice, Inbred C57BL; Mice, Transgenic; Mitogen-Activated Protein Kinases--metabolism--ME; Models, Animal; Monocyte Chemoattractant Protein-1--physiology--PH; Neutrophils --physiology--PH; RANTES--physiology--PH; **Thioredoxin** --administration and dosage--AD; Thioredoxin--genetics--GE

CAS Registry No.: 0 (Lipopolysaccharides); 0 (Monocyte Chemoattractant Protein-1); 0 (RANTES); 52500-60-4 (Thioredoxin)

Enzyme No.: EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.10.- (mitogen-activated protein kinase p38)

Record Date Created: 20011225

Record Date Completed: 20020122

Date of Electronic Publication: 20011211

5/9/5

DIALOG(R)File 155:MEDLINE(R)

09693795 PMID: 8484715

Activation of oxidized cysteine proteinases by thioredoxin-mediated reduction in vitro.

Stephen A G; Powls R; Beynon R J

Department of Biochemistry, University of Liverpool, U.K.

Biochemical journal (ENGLAND) Apr 15 1993, 291 (Pt 2) p345-7, ISSN 0264-6021 Journal Code: 2984726R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Activity of the cysteine adducts of the cysteine proteinases papain and thaumatopain can be recovered by treatment with thioredoxin, thioredoxin reductase and NADPH. Recovery of proteinase activity did not occur if any of the components of the thioredoxin system were omitted, or if thioredoxin or thioredoxin reductase were heat-inactivated. Such an enzyme-mediated process may be of significance in the recovery of cysteine proteinases inactivated by oxidative attack.

Tags: Support, Non-U.S. Gov't

Descriptors: *Cysteine Endopeptidases--metabolism--ME; *Thioredoxin --pharmacology--PD; Enzyme Activation--drug effects--DE; Kinetics; Oxidation-Reduction; Papain--metabolism--ME; Plants--enzymology--EN; **Thioredoxin** --administration and dosage--AD

CAS Registry No.: 52500-60-4 (Thioredoxin)

Enzyme No.: EC 3.4.22 (Cysteine Endopeptidases); EC 3.4.22.- (thaumatopain); EC 3.4.22.2 (Papain)

Record Date Created: 19930601

Record Date Completed: 19930601

?ds

Set	Items	Description
S1	1	'NF KAPPA B'
S2	0	E6 OR E5
S3	12838	E4-E36
S4	13161	R1-R10
S5	5	'THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD'
S6	37	'THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI'
S7	201	'THIOREDOXIN --PHARMACOLOGY --PD'

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S8          8   'THIOREDOXIN --THERAPEUTIC USE --TU'
S9       3248   E3-E32
S10      3248   'THIOREDOXIN' OR DC='D12.776.915.'
S11        54   (S1 OR S2 OR S3 OR S4) AND (S5 OR S6 OR S7 OR S8 OR S9 OR -
                S10)
S12        11   S11/2002:2004
S13        43   S11 NOT S12
S14        12   'CGPC'
?t s8/9/all
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8/9/1

13323835 PMID: 9011676

Amelioration of ischemia-reperfusion injury by human thioredoxin in rabbit lung.

Okubo K; Kosaka S; Isowa N; Hirata T; Hitomi S; Yodoi J; Nakano M; Wada H
Department of Thoracic Surgery, Chest Disease Research Institute, Kyoto University, Japan.

Journal of thoracic and cardiovascular surgery (UNITED STATES) Jan 1997 , 113 (1) p1-9, ISSN 0022-5223 Journal Code: 0376343
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: AIM; INDEX MEDICUS

Human thioredoxin is a polypeptide with thiol groups, possessing reducing activity, which is proved to have the ability to reduce active oxygens. This study evaluated the effect of human thioredoxin on the ischemia-reperfusion lung injury and the roles of human thioredoxin on active oxygens by chemiluminescence examination. The left hilum of the lung of Japanese white rabbits was occluded for 110 minutes and then reperfused for 90 minutes. Ten, 30, 60, and 90 minutes after reperfusion the right hilum was occluded for 5 minutes and the pulmonary functions of the left lung were examined. The animals were divided into four groups, three ischemia groups and a sham group (without occlusion; n = 6). The ischemia groups received human thioredoxin, 60 mg/kg (n = 10), N-acetylcysteine, 150 mg/kg (n = 7), or saline solution (control, n = 10) during reperfusion. Three rabbits in the human thioredoxin group and the control group were used to measure active oxygens with a cypridina luciferin analog. An additional group of reperfused lungs (n = 3) that were given superoxide dismutase after 110 minutes of ischemia was established to identify chemiluminescence examination. Compared with the sham group, reperfusion after 110 minutes of ischemia produced a significant lung injury in the control group. Among the ischemia groups, the human thioredoxin group showed significantly higher arterial oxygen tension at 30, 60, and 90 minutes after reperfusion than the control group, although there was no significant difference between the N-acetylcysteine and control groups. Histologically, intraalveolar exudation, interstitial thickening, and cellular infiltration were seen in the control group, whereas in the thioredoxin group alveolar structure was well preserved. In the measurement of active oxygens the chemiluminescence in the human thioredoxin group was less than that in the control group and as little as that in the group administered superoxide dismutase. We concluded human thioredoxin attenuated ischemia-reperfusion injury by involving active oxygens in rabbit lungs.

Tags: Human; Male
Descriptors: Lung--blood supply--BS; *Reperfusion Injury--drug therapy --DT; * **Thioredoxin** --therapeutic use--TU; Acetylcysteine--therapeutic use --TU; Animals; Chemiluminescence; Lung--pathology--PA; Oxygen--metabolism --ME; Rabbits; Reperfusion Injury--pathology--PA
CAS Registry No.: 52500-60-4 (Thioredoxin); 616-91-1 (Acetylcysteine) ; 7782-44-7 (Oxygen)
Record Date Created: 19970204
Record Date Completed: 19970204

8/9/2
DIALOG(R)File 155:MEDLINE(R)

12856857 PMID: 8545467

Proline, ascorbic acid, or thioredoxin affect jaundice and mortality in Long Evans cinnamon rats.

Hawkins R L; Mori M; Inoue M; Torii K

Torii Nutrient-stasis Project, Research Development Corporation of Japan, Yokohama, Japan.

Pharmacology, biochemistry, and behavior (UNITED STATES) Nov 1995, 52 (3) p509-15, ISSN 0091-3057 Journal Code: 0367050

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The Long Evans Cinnamon (LEC) rat spontaneously develops fulminant hepatitis, which is usually lethal due to excess copper accumulation in the liver and is considered an animal model of Wilson's disease. LEC rats show a strong appetite for proline solution. Daily oral (p.o.) administration of proline resulted in significant delay of mortality. Feeding a copper-deficient diet greatly delayed the onset of jaundice and mortality and voluntary consumption or p.o. administration of proline further delayed jaundice and prevented mortality. LEC rats also consume ascorbic acid solutions, and p.o. administration of ascorbate also results in a significant delay in the appearance of jaundice and mortality. Combined treatment with ascorbic acid and proline is additive to delay further jaundice and mortality. An endogenous antioxidant protein, thioredoxin, when infused by minipump IP, could also inhibit the incidence of jaundice. These results indicate that antioxidant treatment combined with proline may be of benefit in Wilson's disease and possibly other forms of hepatic dysfunction.

Tags: Male

Descriptors: Antioxidants--therapeutic use--TU; *Ascorbic Acid --therapeutic use--TU; *Jaundice--drug therapy--DT; *Proline--therapeutic use--TU; * **Thioredoxin** --therapeutic use--TU; Aging--physiology--PH; Animals; Antioxidants--administration and dosage--AD; Ascorbic Acid --administration and dosage--AD; Copper--deficiency--DF; Diet; Infusion Pumps, Implantable; Jaundice--genetics--GE; Jaundice--mortality--MO; Proline--administration and dosage--AD; Rats; Rats, Inbred Strains; Thioredoxin--administration and dosage--AD

CAS Registry No.: 0 (Antioxidants); 147-85-3 (Proline); 50-81-7 (Ascorbic Acid); 52500-60-4 (Thioredoxin); 7440-50-8 (Copper)

Record Date Created: 19960214

Record Date Completed: 19960214

8/9/3
DIALOG(R)File 155:MEDLINE(R)

12660305 PMID: 7785012

Attenuation of ischaemia reperfusion injury by human thioredoxin.

Fukuse T; Hirata T; Yokomise H; Hasegawa S; Inui K; Mitsui A; Hirakawa T; Hitomi S; Yodoi J; Wada H

Department of Thoracic Surgery, Kyoto University, Japan.

Thorax (ENGLAND) Apr 1995, 50 (4) p387-91, ISSN 0040-6376 Journal Code: 0417353

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

BACKGROUND--Active oxygen species are thought to play a part in ischaemia reperfusion injury. The ability of a novel agent, human thioredoxin (hTRX),

to attenuate lung damage has been examined in a rat model of ischaemia reperfusion injury. METHODS--Twenty eight animals were studied. At thoracotomy the left main bronchus and the left main pulmonary artery were clamped for 75 minutes and the lung was then reperfused for 20 minutes. Phosphate buffered saline was administered intravenously to nine control animals and hTRX (30 micrograms/g body weight) was given intravenously to another group of nine animals. Two experiments were carried out. The first (Exp 1) was a time matched pair experiment (five treated, five controls), and the second (Exp 2) was performed under controlled conditions (four treated, four controls; temperature 25 degrees C, humidity 65%). In another 10 nonischaemic rats and those in Exp 1 biochemical measurements of lipid peroxide, superoxide dismutase, and glutathione peroxide levels were performed. RESULTS--In both experiments rats perfused with hTRX survived longer than controls. In Exp 1 the arterial oxygen tension (PaO2) on air in the hTRX group was higher at 20 minutes than at one minute after reperfusion. In Exp 2 PaO2 at 20 minutes was higher in the hTRX group than in the controls. Lipid peroxide, superoxide dismutase, and glutathione peroxide levels in the control group were higher than in the hTRX group and in the non-ischaemic groups. Histological examination showed less thickening and oedema of the alveolar walls in the hTRX group than in controls. CONCLUSIONS--These results suggest that hTRX is effective as a radical scavenger and can limit the extent of ischaemia reperfusion injury of the lungs of experimental animals.

Tags: Human; Male

Descriptors: Free Radical Scavengers--therapeutic use--TU; *Lung--drug effects--DE; *Reperfusion Injury--drug therapy--DT; * **Thioredoxin** --therapeutic use--TU; Animals; Glutathione Peroxidase--analysis--AN; Lipid Peroxides--analysis--AN; Lung--chemistry--CH; Oxygen--blood--BL; Rats; Rats, Wistar; Reperfusion Injury--blood--BL; Superoxide Dismutase--analysis --AN

CAS Registry No.: 0 (Free Radical Scavengers); 0 (Lipid Peroxides); 52500-60-4 (Thioredoxin); 7782-44-7 (Oxygen)

Enzyme No.: EC 1.11.1.9 (Glutathione Peroxidase); EC 1.15.1.1 (Superoxide Dismutase)

Record Date Created: 19950714

Record Date Completed: 19950714

8/9/4

DIALOG(R)File 155:MEDLINE(R)

11814494 PMID: 12001741

[Thioredoxin and neurodegenerative diseases]

Zhao Lei; Gao Jing

Sheng li ke xue jin zhan Progress in physiology (China) Jan 2002, 33 (1) p74-6, ISSN 0559-7765 Journal Code: 20730140R

Document type: Journal Article; Review; Review, Tutorial

Languages: CHINESE

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

(10 Refs.)

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Alzheimer Disease--metabolism--ME; *Parkinson Disease --metabolism--ME; *Thioredoxin--pharmacology--PD; Animals; Recombinant Proteins--therapeutic use--TU; Thioredoxin--metabolism--ME; **Thioredoxin** --therapeutic use--TU

CAS Registry No.: 0 (Recombinant Proteins); 52500-60-4 (Thioredoxin)

Record Date Created: 20020510

Record Date Completed: 20030116

8/9/5

DIALOG(R)File 155:MEDLINE(R)

11627974 PMID: 11802459

[Retinal neuronal cell death: molecular mechanism and neuroprotection]

Yoshimura N

Department of Ophthalmology, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan.

Nippon Ganka Gakkai zasshi (Japan) Dec 2001, 105 (12) p884-902, ISSN 0029-0203 Journal Code: 7505716

Document type: Journal Article; Review; Review, Multicase ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

In retinitis pigmentosa, retinal detachment, age-related macular degeneration, and glaucoma, retinal neuronal cells are damaged by a common mechanism, apoptosis. Because apoptosis is an active process that requires de novo expression of a "death message", this process can be controlled by inhibiting the expression of the "death message". We first studied whether a retinal ischemia-reperfusion model can be used as a model for retinal neuronal apoptosis. In the retinal ischemia-reperfusion injuries, typical features of apoptosis, including TUNEL-positive cells, DNA ladder formation, and ultrastructural features of apoptosis were found. Using the model, systematic research to identify the "death message" was done by DNA microarray analysis. About 200 messages were found to be up- or down-regulated during the process of retinal ischemia-reperfusion. These genes were divided into four groups: (1) transcription factor genes, (2) cell cycle-related genes, (3) reactive oxygen scavenger genes and (4) molecular chaperon genes. The possible roles of such genes in neuronal apoptosis following retinal ischemia-reperfusion injury were studied. In the model, reactive oxygen species produced by reperfusion was found to generate lipid peroxides and induced up-regulation of a transcription factor, c-Jun, that further induced aberrant expression of cell cycle-related genes such as cyclin D1 in amacrine cells. However, because no controlled expression of cell cycle-related genes takes place in retinal neurons, amacrine cells died by a G1 arrest mechanism. On the other hand, horizontal cells never expressed cyclin D1 and the cells were found to die by necrosis. The study revealed a possible mechanism of retinal neuronal apoptosis and it also became apparent that different types of neurons use different "death messages". Furthermore, the possibility that inhibition of a "death message" sometimes induces necrosis rather than apoptosis was shown. This means that we need to try inhibition of the death mechanism upstream rather than downstream. Administration of thioredoxin, an endogenous reactive oxygen species that blocks generation of lipid peroxides and thus inhibits the death process upstream, was found to be neuroprotective against retinal ischemia-reperfusion injury. Aberrant expression of c-Jun and cyclin D1 was down-regulated by the treatment. Possible roles of caspases were also studied by using the ischemia-reperfusion injury, RCS rat, and excessive light exposure damage in wild type and caspase-1 deficient mice. Also, application of adeno-associated virus that carries Bcl-xL was tested to find possible neuroprotective effects on RCS rats. Our studies showed that caspase-1 played a more important role in the retinal photoreceptors and caspase-3 was important in neurons in the inner nuclear layer. Caspase-2 was found to be a major caspase in the retinal ganglion cell layer. In agreement with the findings, caspase-1 deficient mice showed less prominent light damage than wild type mice. Gene therapy by Bcl-xL was effective to protect retinal photoreceptor damage in RCS rats. (59 Refs.)

Descriptors: *Apoptosis; *Reperfusion Injury--pathology--PA; *Retinal Diseases--pathology--PA; *Retinal Vessels--pathology--PA; Animals; Genes, cdc; In Situ Nick-End Labeling; Necrosis; Oligonucleotide Array Sequence Analysis; Rats; **Thioredoxin** --therapeutic use--TU

CAS Registry No.: 52500-60-4 (Thioredoxin)

Record Date Created: 20020122

Record Date Completed: 20020205

DIALOG(R)File 155:MEDLINE(R)

11554671 PMID: 11726031

Redox control of cellular function by thioredoxin; a new therapeutic direction in host defence.

Nishinaka Y; Nakamura H; Masutani H; Yodoi J

Department of Biological Responses, Institute for Virus Research, Kyoto University, Sakyo, Japan.

Archivum immunologiae et therapiae experimentalis (Poland) 2001, 49 (4) p285-92, ISSN 0004-069X Journal Code: 0114365

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Compelling evidence has suggested that oxidative stress mediates various cellular responses, and control of reduction/oxidation (redox) is important in maintaining the homeostasis of an organism. The thioredoxin (TRX) system, as well as the glutathione system, is one of the key systems in controlling cellular redox status. TRX is a small ubiquitous protein with the redox-active site sequence -Cys-Gly-Pro-Cys-. It has been demonstrated to be a multifunctional protein, which has regulatory roles in cellular signaling and gene transcription in addition to cytoprotective activities through the quenching of reactive oxygen species. Various oxidative stimuli, such as UV irradiation, cytokines and some chemicals, promptly induce the expression of TRX. Overexpression of TRX correlates with a wide variety of oxidative stress conditions and, in some cases, TRX has shown promising effects for clinical use, for instance in the attenuation of tissue injury in ischemia reperfusion models. The modulation of TRX functions in association with other redox-regulatory molecules should give us a new therapeutic strategy in the treatment of oxidative stress-mediated disorders and diseases. (60 Refs.)

Tags: Human; In Vitro; Support, Non-U.S. Gov't

Descriptors: Thioredoxin--metabolism--ME; * **Thioredoxin** --therapeutic use--TU; Animals; Apoptosis--drug effects--DE; Carrier Proteins--metabolism --ME; Intracellular Fluid--metabolism--ME; Neoplasms--drug therapy--DT; Neoplasms--metabolism--ME; Neoplasms--pathology--PA; Oxidation-Reduction; Oxidative Stress; Reactive Oxygen Species--metabolism--ME; Signal Transduction; Thioredoxin--immunology--IM

CAS Registry No.: 0 (Carrier Proteins); 0 (Reactive Oxygen Species); 52500-60-4 (Thioredoxin)

Record Date Created: 20011129

Record Date Completed: 20020528

8/9/7

DIALOG(R)File 155:MEDLINE(R)

10875226 PMID: 11006259

Lipid peroxidation and peroxynitrite in retinal ischemia-reperfusion injury.

Shibuki H; Katai N; Yodoi J; Uchida K; Yoshimura N

Department of Ophthalmology, Shinshu University School of Medicine, Matsumoto, Japan.

Investigative ophthalmology & visual science (UNITED STATES) Oct 2000, 41 (11) p3607-14, ISSN 0146-0404 Journal Code: 7703701

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

PURPOSE: To investigate whether lipid peroxides play a role in retinal cell death due to ischemia-reperfusion injury, whether recombinant human thioredoxin (rhTRX) treatment reduces production of lipid peroxides of the retina, and whether such treatment reduces the number of cells expressing

c-Jun and cyclin D1. METHODS: Retinal ischemia was induced in rats by increasing the intraocular pressure to 110 mm Hg for 60 minutes. After reperfusion, immunohistochemical staining for lipid peroxide, peroxynitrite, c-Jun, and cyclin D1 and propidium iodide (PI) staining were performed on retinal sections from animals treated intravenously with and without rhTRX, a free radical scavenger. Quantitative analyses of PI-, c-Jun-, and cyclin D1-positive cells were performed after the ischemic insult. Concentration of lipid peroxides in the retina was determined by the thiobarbituric acid assay. RESULTS: Specific immunostaining for lipid peroxides was seen in the ganglion cell layer at 6 hours after reperfusion, in the inner nuclear layer at 12 hours, and in the outer nuclear layer at 48 hours. Time course studies for PI-positive cells in the three nuclear layers coincided with those of specific immunostaining for lipid peroxides. The specific immunostaining was weakened by pre- and posttreatment with 0.5 mg of rhTRX. The number of PI-, c-Jun-, and cyclin D1-positive cells and the concentration of lipid peroxides were significantly decreased by treatment with rhTRX compared with those of vehicle-treated control rats (P: < 0. 01). CONCLUSIONS: Lipid peroxides formed by free radicals may play a role in neuronal cell death in retinal ischemia-reperfusion injury.

Tags: Male; Support, Non-U.S. Gov't

Descriptors: *Lipid Peroxidation; *Lipid Peroxides--metabolism--ME; *Nitrates--metabolism--ME; *Reperfusion Injury--metabolism--ME; *Retina --metabolism--ME; *Retinal Diseases--metabolism--ME; Aldehydes--metabolism --ME; Animals; Cell Death; Cyclin D1--metabolism--ME; Fluorescent Antibody Technique, Indirect; Free Radical Scavengers--therapeutic use--TU; Propidium--metabolism--ME; Proto-Oncogene Proteins c-jun--metabolism--ME; Rats; Rats, Sprague-Dawley; Recombinant Proteins--therapeutic use--TU; Reperfusion Injury--drug therapy--DT; Reperfusion Injury--pathology--PA; Retina--pathology--PA; Retinal Diseases--drug therapy--DT; Retinal Diseases--pathology--PA; Thiobarbituric Acid Reactive Substances; **Thioredoxin** --therapeutic use--TU

CAS Registry No.: 0 (Aldehydes); 0 (Free Radical Scavengers); 0 (Lipid Peroxides); 0 (Nitrates); 0 (Proto-Oncogene Proteins c-jun); 0 (Recombinant Proteins); 0 (Thiobarbituric Acid Reactive Substances); 136601-57-5 (Cyclin D1); 26404-66-0 (peroxynitric acid); 29343-52-0 (4-hydroxy-2-nonenal); 36015-30-2 (Propidium); 52500-60-4 (Thioredoxin)

Record Date Created: 20001012

Record Date Completed: 20001012

8/9/8

DIALOG(R)File 155:MEDLINE(R)

10281312 PMID: 7979362

Thioredoxin: a multifunctional regulatory protein with a bright future in technology and medicine.

Buchanan B B; Schurmann P; Decottignies P; Lozano R M

Department of Plant Biology, University of California, Berkeley 94720.

Archives of biochemistry and biophysics (UNITED STATES) Nov 1 1994, 314 (2) p257-60, ISSN 0003-9861 Journal Code: 0372430

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

Thioredoxins are proteins, typically with a molecular mass of 12 kDa, that are widely, if not universally, distributed in the animal, plant, and bacterial kingdoms. Thioredoxins undergo reversible redox change through a disulfide group (S-S-->2 SH). Two cellular reductants--reduced ferredoxin and NADPH--supply the equivalents for reduction via different enzymes. The nature of the reductant serves as a basis for distinguishing and naming the two thioredoxin systems, which are discussed below in relation to their possible application in technology and medicine. Most of the discussion is referenced by general reviews. In the section dealing with animal cells, however, much of the material is quite recent. Thus, there, and elsewhere to a lesser extent, previously uncited studies are assigned specific

references. (23 Refs.)
  Tags: Human
  Descriptors: Thioredoxin--metabolism--ME; * **Thioredoxin** --therapeutic use--TU; Animals; Embryo and Fetal Development; Ferredoxins--metabolism--ME; NADP--metabolism--ME; Plants--cytology--CY; Plants--metabolism--ME
  CAS Registry No.: 0 (Ferredoxins); 52500-60-4 (Thioredoxin); 53-59-8 (NADP)
  Record Date Created: 19941207
  Record Date Completed: 19941207
?logoff hold
       03sep04 14:33:39 User228206 Session D2225.2
           $13.15   4.110 DialUnits File155
              $14.28 68 Type(s) in Format 9
           $14.28 68 Types
    $27.43 Estimated cost File155
     $1.50 TELNET
    $28.93 Estimated cost this search
    $28.93 Estimated total session cost   4.307 DialUnits

Status: Signed Off. (6 minutes)

```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009998...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 04.12.02D

Last logoff:  03sep04 14:07:26
Logon file405 03sep04 14:27:59
* * * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                     *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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      /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
?b 155

       03sep04 14:28:00 User228206 Session D2225.1
            $0.00    0.197 DialUnits FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.197 DialUnits


File 155:MEDLINE(R) 1951-2004/Aug W5
       (c) format only 2004 The Dialog Corp.
*File 155: Medline has been reloaded. Accession numbers
have changed. Please see HELP NEWS 154 for details.

      Set  Items  Description
      ---  -----  -----------
?e nf-kappab

Ref   Items   RT  Index-term
E1      791       NF-KAPPA B P65
E2        0    1  NF-KAPPA B-BINDING SITE, HIV
```

```
E3        0      *NF-KAPPAB
E4     1500       NF-KAPPAB INHIBITOR ALPHA
E5        2       NF-KB
E6        1       NF-KB2
E7        8       NF-L
E8        5       NF-M
E9        1       NF-M13 PROTEIN
E10       1       NF-M17 PROTEIN
E11       2       NF-PROTOCADHERIN
E12       2       NF-YA

          Enter P or PAGE for more
?e nf kappa

Ref   Items  Index-term
E1        2  NE97
E2    23639  NF
E3        0 *NF KAPPA
E4        1  NF KAPPA B
E5        1  NF PROTOCOL
E6        1  NF SUB &KGR; B
E7        7  NF 279
E8        1  NF 307
E9        1  NF 6505
E10       1  NF 86II
E11       1  NF 86II SULFATE
E12       3  NF&KGR;B

          Enter P or PAGE for more
?s e4
      S1       1  'NF KAPPA B'
?e e2
>>>No related terms exist for this term
?e nf-kappab

Ref   Items   RT  Index-term
E1      791       NF-KAPPA B P65
E2        0    1  NF-KAPPA B-BINDING SITE, HIV
E3        0      *NF-KAPPAB
E4     1500       NF-KAPPAB INHIBITOR ALPHA
E5        2       NF-KB
E6        1       NF-KB2
E7        8       NF-L
E8        5       NF-M
E9        1       NF-M13 PROTEIN
E10       1       NF-M17 PROTEIN
E11       2       NF-PROTOCADHERIN
E12       2       NF-YA

          Enter P or PAGE for more
?e e2

Ref   Items Type  RT  Index-term
R1        0        1 *NF-KAPPA B-BINDING SITE, HIV
R2       72   X   10  HIV ENHANCER
?s e6 or e5
>>>"E6" does not exist
>>>"E5" does not exist
               0  E6
               0  E5
      S2       0  E6 OR E5
?e nf-kappa

Ref   Items   RT  Index-term
E1        3       NF-IL3A PROTEIN
E2        4    1  NF-IL6
E3        0      *NF-KAPPA
```

```
E4    12809   12  NF-KAPPA B
E5        4       NF-KAPPA B --ADMINISTRATION AND DOSAGE --AD
E6        2       NF-KAPPA B --ADVERSE EFFECTS --AE
E7       16       NF-KAPPA B --AGONISTS --AG
E8        1       NF-KAPPA B --ANALOGS AND DERIVATIVES --AA
E9      231       NF-KAPPA B --ANALYSIS --AN
E10    2019       NF-KAPPA B --ANTAGONISTS AND INHIBITORS --AI
E11     577       NF-KAPPA B --BIOSYNTHESIS --BI
E12      54       NF-KAPPA B --BLOOD --BL

          Enter P or PAGE for more
?p

Ref   Items  Index-term
E13       1  NF-KAPPA B --CEREBROSPINAL FLUID --CF
E14     309  NF-KAPPA B --CHEMISTRY --CH
E15       5  NF-KAPPA B --CLASSIFICATION --CL
E16      70  NF-KAPPA B --DEFICIENCY --DF
E17       1  NF-KAPPA B --DIAGNOSTIC USE --DU
E18     502  NF-KAPPA B --DRUG EFFECTS --DE
E19    1799  NF-KAPPA B --GENETICS --GE
E20     283  NF-KAPPA B --IMMUNOLOGY --IM
E21      68  NF-KAPPA B --ISOLATION AND PURIFICATION --IP
E22    9087  NF-KAPPA B --METABOLISM --ME
E23       1  NF-KAPPA B --PHARMACOKINETICS --PK
E24     139  NF-KAPPA B --PHARMACOLOGY --PD

          Enter P or PAGE for more
?p

Ref   Items   RT  Index-term
E25    1949       NF-KAPPA B --PHYSIOLOGY --PH
E26      60       NF-KAPPA B --RADIATION EFFECTS --RE
E27       1       NF-KAPPA B --SECRETION --SE
E28       9       NF-KAPPA B --THERAPEUTIC USE --TU
E29       1       NF-KAPPA B --TOXICITY --TO
E30       3       NF-KAPPA B --ULTRASTRUCTURE --UL
E31       1       NF-KAPPA B --URINE --UR
E32     160       NF-KAPPA B KINASE
E33      58       NF-KAPPA B P105 PRECURSOR
E34     392       NF-KAPPA B P50
E35     791       NF-KAPPA B P65
E36       0    1  NF-KAPPA B-BINDING SITE, HIV

          Enter P or PAGE for more
?s e4-e36
          12809  NF-KAPPA B
              4  NF-KAPPA B --ADMINISTRATION AND DOSAGE --AD
              2  NF-KAPPA B --ADVERSE EFFECTS --AE
             16  NF-KAPPA B --AGONISTS --AG
              1  NF-KAPPA B --ANALOGS AND DERIVATIVES --AA
            231  NF-KAPPA B --ANALYSIS --AN
           2019  NF-KAPPA B --ANTAGONISTS AND INHIBITORS --AI
            577  NF-KAPPA B --BIOSYNTHESIS --BI
             54  NF-KAPPA B --BLOOD --BL
              1  NF-KAPPA B --CEREBROSPINAL FLUID --CF
            309  NF-KAPPA B --CHEMISTRY --CH
              5  NF-KAPPA B --CLASSIFICATION --CL
             70  NF-KAPPA B --DEFICIENCY --DF
              1  NF-KAPPA B --DIAGNOSTIC USE --DU
            502  NF-KAPPA B --DRUG EFFECTS --DE
           1799  NF-KAPPA B --GENETICS --GE
            283  NF-KAPPA B --IMMUNOLOGY --IM
             68  NF-KAPPA B --ISOLATION AND PURIFICATION --IP
           9087  NF-KAPPA B --METABOLISM --ME
              1  NF-KAPPA B --PHARMACOKINETICS --PK
            139  NF-KAPPA B --PHARMACOLOGY --PD
```

```
             1949  NF-KAPPA B --PHYSIOLOGY --PH
               60  NF-KAPPA B --RADIATION EFFECTS --RE
                1  NF-KAPPA B --SECRETION --SE
                9  NF-KAPPA B --THERAPEUTIC USE --TU
                1  NF-KAPPA B --TOXICITY --TO
                3  NF-KAPPA B --ULTRASTRUCTURE --UL
                1  NF-KAPPA B --URINE --UR
              160  NF-KAPPA B KINASE
               58  NF-KAPPA B P105 PRECURSOR
              392  NF-KAPPA B P50
              791  NF-KAPPA B P65
                0  NF-KAPPA B-BINDING SITE, HIV
      S3    12838  E4-E36
?p

Ref    Items  Index-term
E37     1500  NF-KAPPAB INHIBITOR ALPHA
E38        2  NF-KB
E39        1  NF-KB2
E40        8  NF-L
E41        5  NF-M
E42        1  NF-M13 PROTEIN
E43        1  NF-M17 PROTEIN
E44        2  NF-PROTOCADHERIN
E45        2  NF-YA
E46       16  NF-YA PROTEIN
E47        2  NF-YB
E48       10  NF-YB PROTEIN

          Enter P or PAGE for more
?e e4

Ref    Items Type  RT  Index-term
R1     12809       12 *NF-KAPPA B
R2     12809   X      DC=D12.776.260.600. (NF-KAPPA B)
R3     12809   X      DC=D12.776.660.600. (NF-KAPPA B)
R4     12809   X      DC=D12.776.930.600. (NF-KAPPA B)
R5         0   X    1  IMMUNOGLOBULIN ENHANCER-BINDING PROTEIN
R6         0   X    1  KAPPA B ENHANCER BINDING PROTEIN
R7         0   X    1  NUCLEAR FACTOR KAPPA B
R8         0   X    1  TRANSCRIPTION FACTOR NF-KB
R9        72   R   10  HIV ENHANCER
R10     2113   R    4  I-KAPPA B
R11    68819   B   72  DNA-BINDING PROTEINS
R12    27894   B   51  NUCLEAR PROTEINS

          Enter P or PAGE for more
?p

Ref    Items Type  RT  Index-term
R13    63230   B   59  TRANSCRIPTION FACTORS
?s r1-r10
           12809  NF-KAPPA B
           12809  DC=D12.776.260.600.  (NF-KAPPA B)
           12809  DC=D12.776.660.600.  (NF-KAPPA B)
           12809  DC=D12.776.930.600.  (NF-KAPPA B)
               0  IMMUNOGLOBULIN ENHANCER-BINDING PROTEIN
               0  KAPPA B ENHANCER BINDING PROTEIN
               0  NUCLEAR FACTOR KAPPA B
               0  TRANSCRIPTION FACTOR NF-KB
              72  HIV ENHANCER
            2113  I-KAPPA B
      S4   13161  R1-R10
?ds

Set     Items   Description
S1          1   'NF KAPPA B'
```

```
S2          0   E6 OR E5
S3      12838   E4-E36
S4      13161   R1-R10
?e thioredoxin

Ref    Items    RT  Index-term
E1         1        THIOREDIXIN
E2         1        THIOREDOX
E3      3248     1 *THIOREDOXIN
E4         2        THIOREDOXIN (80-84)
E5         5        THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD
E6         2        THIOREDOXIN --ANALOGS AND DERIVATIVES --AA
E7        82        THIOREDOXIN --ANALYSIS --AN
E8        37        THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI
E9       109        THIOREDOXIN --BIOSYNTHESIS --BI
E10       47        THIOREDOXIN --BLOOD --BL
E11        3        THIOREDOXIN --CHEMICAL SYNTHESIS --CS
E12      467        THIOREDOXIN --CHEMISTRY --CH

          Enter P or PAGE for more
?p

Ref    Items  Index-term
E13       10  THIOREDOXIN --CLASSIFICATION --CL
E14       11  THIOREDOXIN --DRUG EFFECTS --DE
E15      584  THIOREDOXIN --GENETICS --GE
E16       30  THIOREDOXIN --IMMUNOLOGY --IM
E17      105  THIOREDOXIN --ISOLATION AND PURIFICATION --IP
E18      926  THIOREDOXIN --METABOLISM --ME
E19        1  THIOREDOXIN --PHARMACOKINETICS --PK
E20      201  THIOREDOXIN --PHARMACOLOGY --PD
E21        9  THIOREDOXIN --PHYSIOLOGY --PH
E22        2  THIOREDOXIN --RADIATION EFFECTS --RE
E23       14  THIOREDOXIN --SECRETION --SE
E24        8  THIOREDOXIN --THERAPEUTIC USE --TU

          Enter P or PAGE for more
?p

Ref    Items    RT  Index-term
E25        2        THIOREDOXIN --ULTRASTRUCTURE --UL
E26        1        THIOREDOXIN --URINE --UR
E27        3        THIOREDOXIN CH2
E28        1        THIOREDOXIN C3
E29       36        THIOREDOXIN F
E30        5        THIOREDOXIN GLUTATHIONE REDUCTASE
E31       18        THIOREDOXIN H
E32        5        THIOREDOXIN H2 PROTEIN, PLANT
E33      600     2  THIOREDOXIN REDUCTASE (NADPH)
E34       27        THIOREDOXIN REDUCTASE (NADPH) --ANALYSIS --AN
E35       61        THIOREDOXIN REDUCTASE (NADPH) --ANTAGONISTS AN
E36       34        THIOREDOXIN REDUCTASE (NADPH) --BIOSYNTHESIS -

          Enter P or PAGE for more
?s e5
      S5        5  'THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD'
?s e8
      S6       37  'THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI'
?s e20
      S7      201  'THIOREDOXIN --PHARMACOLOGY --PD'
?s e24
      S8        8  'THIOREDOXIN --THERAPEUTIC USE --TU'
?s e3-e32
             3248  THIOREDOXIN
                2  THIOREDOXIN (80-84)
                5  THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD
                2  THIOREDOXIN --ANALOGS AND DERIVATIVES --AA
```

```
              82  THIOREDOXIN --ANALYSIS --AN
              37  THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI
             109  THIOREDOXIN --BIOSYNTHESIS --BI
              47  THIOREDOXIN --BLOOD --BL
               3  THIOREDOXIN --CHEMICAL SYNTHESIS --CS
             467  THIOREDOXIN --CHEMISTRY --CH
              10  THIOREDOXIN --CLASSIFICATION --CL
              11  THIOREDOXIN --DRUG EFFECTS --DE
             584  THIOREDOXIN --GENETICS --GE
              30  THIOREDOXIN --IMMUNOLOGY --IM
             105  THIOREDOXIN --ISOLATION AND PURIFICATION --IP
             926  THIOREDOXIN --METABOLISM --ME
               1  THIOREDOXIN --PHARMACOKINETICS --PK
             201  THIOREDOXIN --PHARMACOLOGY --PD
               9  THIOREDOXIN --PHYSIOLOGY --PH
               2  THIOREDOXIN --RADIATION EFFECTS --RE
              14  THIOREDOXIN --SECRETION --SE
               8  THIOREDOXIN --THERAPEUTIC USE --TU
               2  THIOREDOXIN --ULTRASTRUCTURE --UL
               1  THIOREDOXIN --URINE --UR
               3  THIOREDOXIN CH2
               1  THIOREDOXIN C3
              36  THIOREDOXIN F
               5  THIOREDOXIN GLUTATHIONE REDUCTASE
              18  THIOREDOXIN H
               5  THIOREDOXIN H2 PROTEIN, PLANT
      S9     3248  E3-E32
?e e3

Ref    Items Type  RT  Index-term
R1      3248         1 *THIOREDOXIN
R2      1846   X        DC=D12.776.915. (THIOREDOXIN)
?s r1 or r2
            3248  THIOREDOXIN
            1846  DC=D12.776.915.  (THIOREDOXIN)
     S10    3248  'THIOREDOXIN' OR DC='D12.776.915.'
?ds

Set     Items   Description
S1          1   'NF KAPPA B'
S2          0   E6 OR E5
S3      12838   E4-E36
S4      13161   R1-R10
S5          5   'THIOREDOXIN --ADMINISTRATION AND DOSAGE --AD'
S6         37   'THIOREDOXIN --ANTAGONISTS AND INHIBITORS --AI'
S7        201   'THIOREDOXIN --PHARMACOLOGY --PD'
S8          8   'THIOREDOXIN --THERAPEUTIC USE --TU'
S9       3248   E3-E32
S10      3248   'THIOREDOXIN' OR DC='D12.776.915.'
?s (s1 or s2 or s3 or s4) and (s5 or s6 or s7 or s8 or s9 or s10)
               1  S1
               0  S2
           12838  S3
           13161  S4
               5  S5
              37  S6
             201  S7
               8  S8
            3248  S9
            3248  S10
     S11      54  (S1 OR S2 OR S3 OR S4) AND (S5 OR S6 OR S7 OR S8 OR S9 OR
                  S10)
?s s11/2002:2004
              54  S11
         1483088  PY=2002 : PY=2004
     S12      11  S11/2002:2004
?s s11 not s12
```

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Search Swiss-Prot/TrEMBL for thioredoxin helicobacter Go Clear

==========

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In case of problems, please read the online BLAST help.
If your question is not covered, please contact <helpdesk@expasy.org>.

NCBI BLAST program reference [PMID:9254694]:
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

==========

Query length: 106 AA
Date run: 2004-09-03 15:26:05 UTC+0100 on sib-gm1.unil.ch
Program: NCBI BLASTP 1.5.4-Paracel [2003-06-05]
Database: EXPASY/UniProt
1,544,870 sequences; 494,584,931 total letters

Taxonomic view | NiceBlast view | Printable view

List of potentially matching sequences

Send selected sequences to Clustal W (multiple alignment) Submit Query
Select up to...

☐ Include query sequence

	Db	AC	Description	Score	E-value
☐	sp	P56430	THIO_HELPY Thioredoxin (TRX) [trxA] [Helicobacter pylo...	216	5e-56
☐	tr	Q7MSG6	THIOREDOXIN [TRXA] [Wolinella succinogenes]	157	4e-38
☐	tr	Q9PIY0	Thioredoxin [trxA] [Campylobacter jejuni]	155	1e-37
☐	tr	Q7VK37	Thioredoxin [trxA_2] [Helicobacter hepaticus]	146	8e-35
☐	tr	Q9RVS8	Thioredoxin [DR0944] [Deinococcus radiodurans]	120	3e-27
☐	tr	Q8EPI6	Thioredoxin [OB2117] [Oceanobacillus iheyensis]	119	8e-27
☐	sp	Q8CPL5	THIO_STAEP Thioredoxin (TRX) [trxA] [Staphylococcus ep...	116	7e-26
☐	sp	Q9ZEH4	THIO_STAAM Thioredoxin (TRX) [trxA] [Staphylococcus au...	116	9e-26
☐	sp	P14949	THIO_BACSU Thioredoxin (TRX) [trxA] [Bacillus subtilis]	116	9e-26
☐	tr	Q7MXW5	Thioredoxin [trx] [Porphyromonas gingivalis (Bacteroid...	116	9e-26

☐	tr Q6GHU0	Thioredoxin [trxA] [Staphylococcus aureus subsp. aureu...	116	9e-26
☐	tr Q6GA69	Thioredoxin [SAS1079] [Staphylococcus aureus subsp. au...	116	9e-26
☐	sp Q8KE49	THI2_CHLTE Thioredoxin 2 (Trx-2) [trx2] [Chlorobium te...	115	1e-25
☐	tr Q9KWL9	Thioredoxin [Staphylococcus warneri]	115	1e-25
☐	tr Q9K8A8	Thioredoxin [trxA] [Bacillus halodurans]	114	3e-25
☐	sp P37395	THIO_CYACA Thioredoxin [trxA] [Cyanidium caldarium]	113	6e-25
☐	tr Q72B01	Thioredoxin [trx] [Desulfovibrio vulgaris (strain Hild...	112	1e-24
☐	tr Q7VBF6	Thioredoxin family protein [trxA] [Prochlorococcus mar...	111	2e-24
☐	sp P06544	THI1_ANASP Thioredoxin 1 (TRX-1) (Thioredoxin M) [trxA...	110	4e-24
☐	tr Q8DKP7	Thioredoxin [tll0812] [Synechococcus elongatus (Thermo...	110	4e-24
☐	sp P43785	THIO_HAEIN Thioredoxin (TRX) [trxA] [Haemophilus influ...	109	8e-24
☐	tr Q6LLL6	Putative thioredoxin [SO0406] [Photobacterium profundu...	109	1e-23
☐	tr Q8ZAD9	Thioredoxin 1 [trxA] [Yersinia pestis]	109	1e-23
☐	tr Q8A5L0	Thioredoxin (Thioredoxin M) [BT2229] [Bacteroides thet...	109	1e-23
☐	sp Q9X2T1	THIO_PSEAE Thioredoxin (TRX) [trxA] [Pseudomonas aerug...	108	1e-23
☐	sp P00274	THIO_ECOLI Thioredoxin 1 (TRX1) (TRX) [trxA] [Escheric...	108	2e-23
☐	tr Q9KV51	Thioredoxin [VC0306] [Vibrio cholerae]	108	2e-23
☐	tr Q9RYY9	Thioredoxin 1 [DRA0164] [Deinococcus radiodurans]	108	2e-23
☐	sp P48384	THIM_PEA Thioredoxin M-type, chloroplast precursor (TR...	108	2e-23
☐	tr Q87KH6	Thioredoxin [VP3001] [Vibrio parahaemolyticus]	108	2e-23
☐	tr Q9CF37	Thioredoxin [trxA] [Lactococcus lactis (subsp. lactis)...	107	3e-23
☐	tr Q7VKR2	Thioredoxin [trxA] [Haemophilus ducreyi]	107	3e-23
☐	tr Q7NM87	Thioredoxin [gll0880] [Gloeobacter violaceus]	107	3e-23
☐	sp P50254	THIO_PORYE Thioredoxin [trxA] [Porphyra yezoensis]	107	4e-23
☐	sp Q9ZP20	THIM_ORYSA Thioredoxin M-type, chloroplast precursor (...	107	4e-23
☐	tr Q97EM7	Thioredoxin [CAC3083] [Clostridium acetobutylicum]	107	4e-23
☐	tr Q7V6M6	Thioredoxin [trxA] [Prochlorococcus marinus (strain MI...	107	5e-23
☐	sp P51225	THIO_PORPU Thioredoxin [trxA] [Porphyra purpurea]	106	7e-23
☐	sp Q9ZP21	THIM_WHEAT Thioredoxin M-type, chloroplast precursor (...	106	7e-23
☐	tr Q6CZE0	Thioredoxin [ECA4212] [Erwinia carotovora subsp. atros...	106	7e-23
☐	tr Q7CET1	Putative thioredoxin [trx.2] [Streptococcus pyogenes (...	106	9e-23
☐	tr Q99Y75	Putative thioredoxin [trx] [Streptococcus pyogenes]	106	9e-23
☐	tr Q8NZI7	Putative thioredoxin [trxA] [Streptococcus pyogenes (s...	106	9e-23
☐	tr Q8E3J7	Hypothetical protein gbs1762 [gbs1762] [Streptococcus ...	106	9e-23
☐	tr Q8DXX8	Thioredoxin [trx] [Streptococcus agalactiae (serotype V)]	106	9e-23
☐	tr Q879K6	Putative thioredoxin [SPs0281] [Streptococcus pyogenes...	106	9e-23
☐	tr Q7NXP2	Thioredoxin [trxA] [Chromobacterium violaceum]	106	9e-23
☐	sp P52231	THIO_SYNY3 Thioredoxin (TRX) [trxA] [Synechocystis sp....	105	1e-22
☐	sp P12243	THI1_SYNP7 Thioredoxin 1 (TRX-1) (Thioredoxin M) [trxA...	105	1e-22
☐	sp P00275	THI1_CORNE Thioredoxin C-1 [Corynebacterium nephridii]	105	1e-22
☐	tr Q8YVV7	Thioredoxin [all1866] [Anabaena sp. (strain PCC 7120)]	105	1e-22
☐	tr Q8DDN7	Thioredoxin [VV10938] [Vibrio vulnificus]	105	1e-22
☐	tr Q7MGP8	Thiol-disulfide isomerase and thioredoxin [VV3182] [Vi...	105	1e-22
☐	tr O67747	Thioredoxin [trxA1] [Aquifex aeolicus]	105	1e-22
☐	tr O28984	Thioredoxin (Trx-3) [AF1284] [Archaeoglobus fulgidus]	105	2e-22

☐	tr Q7V126	Thioredoxin [trxA] [Prochlorococcus marinus subsp. pas...	104	3e-22
☐	tr Q7UJ35	Thioredoxin 1 [trxA] [Rhodopirellula baltica]	104	3e-22
☐	tr Q7MYL3	Thioredoxin 1 (TRX1) (TRX) [trxA] [Photorhabdus lumine...	104	3e-22
☐	tr Q7U898	Thioredoxin [trxA] [Synechococcus sp. (strain WH8102)]	104	3e-22
☐	tr Q95AH9	Putative thioredoxin m2 [trxm2] [Pisum sativum (Garden...	104	3e-22
☐	sp Q9S386	THIO_LISMO Thioredoxin (Trx) [trxA] [Listeria monocyto...	103	4e-22
☐	tr Q720J6	Thioredoxin [trx-1] [Listeria monocytogenes (serotype ...	103	4e-22
☐	tr Q8YE56	THIOREDOXIN C-1 [BMEI2022] [Brucella melitensis]	103	6e-22
☐	tr Q8FXY9	Thioredoxin [trx-1] [Brucella suis]	103	6e-22
☐	tr Q835H2	Thioredoxin [trx] [Enterococcus faecalis (Streptococcu...	103	6e-22
☐	sp P33791	THIO_STRAU Thioredoxin (TRX) (Fragment) [trxA] [Strept...	103	7e-22
☐	tr Q6G588	Thioredoxin [trxA] [Bartonella henselae (Rochalimaea h...	103	7e-22
☐	sp P07591	THIM_SPIOL Thioredoxin M-type, chloroplast precursor (...	102	1e-21
☐	sp Q41864	THIM_MAIZE Thioredoxin M-type, chloroplast precursor (...	102	1e-21
☐	tr Q81L73	Thioredoxin [trx] [Bacillus anthracis]	102	1e-21
☐	tr Q817L8	Thioredoxin [BC4521] [Bacillus cereus (strain ATCC 145...	102	1e-21
☐	tr Q72ZM0	Thioredoxin [trx] [Bacillus cereus (strain ATCC 10987)]	102	1e-21
☐	tr Q6HD04	Thioredoxin [trxA] [Bacillus thuringiensis serovar kon...	102	1e-21
☐	tr Q8EJQ6	Thioredoxin 1 [trxA] [Shewanella oneidensis]	102	2e-21
☐	tr Q8DSD2	Putative thioredoxin [trxA] [Streptococcus mutans]	102	2e-21
☐	tr Q8L1N0	Thioredoxin [trxA] [Buchnera aphidicola (subsp. Pemphi...	102	2e-21
☐	tr Q8P4D3	Thioredoxin [trxA] [Xanthomonas campestris (pv. campes...	101	2e-21
☐	tr Q7M0Y9	Thioredoxin [Clostridium pasteurianum]	101	2e-21
☐	tr Q88CG6	Thioredoxin [trx-2] [Pseudomonas putida (strain KT2440)]	101	3e-21
☐	tr Q83A24	Thioredoxin [trx] [Coxiella burnetii]	100	4e-21
☐	tr Q72HU9	Thioredoxin [TTC1385] [Thermus thermophilus (strain HB...	100	4e-21
☐	tr Q8UJA6	Thioredoxin C-1 [trxA] [Agrobacterium tumefaciens (str...	100	6e-21
☐	tr Q97P68	Thioredoxin [SP1776] [Streptococcus pneumoniae]	100	6e-21
☐	tr Q7D2B9	AGR_C_37p [AGR_C_37] [Agrobacterium tumefaciens (strai...	100	6e-21
☐	sp Q92JR5	THIO_RICCN Thioredoxin (TRX) [trxA] [Rickettsia conorii]	100	8e-21
☐	tr Q8DNP9	Thioredoxin reductase (EC 1.6.4.5) [trxA] [Streptococc...	100	8e-21
☐	tr Q7PAB0	Thioredoxin [rsib_orf.717] [Rickettsia sibirica]	100	8e-21
☐	tr Q9JYY9	Thioredoxin [NMB1366] [Neisseria meningitidis (serogro...	99	1e-20
☐	tr Q87UQ3	Thioredoxin [trx-2] [Pseudomonas syringae (pv. tomato)]	99	1e-20
☐	sp P80579	THIO_ALIAC Thioredoxin (TRX) [trxA] [Alicyclobacillus ...	99	1e-20
☐	tr Q8RAI5	Thiol-disulfide isomerase and thioredoxins [TrxA2] [Th...	99	1e-20
☐	tr Q8PFZ2	Thioredoxin [trxA] [Xanthomonas axonopodis (pv. citri)]	99	1e-20
☐	tr Q8F4W0	Thioredoxin (TRX) [trxA] [Leptospira interrogans]	99	1e-20
☐	tr Q72QY0	Thioredoxin [trxA] [Leptospira interrogans (serogroup ...	99	1e-20
☐	tr Q6ME96	Probable thioredoxin [trxA] [Parachlamydia sp. (strain...	99	1e-20
☐	sp Q9CM49	THIO_PASMU Thioredoxin (TRX) [trxA] [Pasteurella multo...	99	2e-20
☐	sp Q7M1B9	THIO_CHLAU Thioredoxin (TRX) [trxA] [Chloroflexus aura...	99	2e-20
☐	tr Q8ZMX4	Thioredoxin 2, redox factor [trxC] [Salmonella typhimu...	99	2e-20
☐	tr Q9JTY5	Thioredoxin I [trxA] [Neisseria meningitidis (serogrou...	99	2e-20
☐	tr Q8NL58	Thiol-disulfide isomerase and thioredoxins [Cgl3091] [...	99	2e-20

Graphical overview of the alignments

Click here to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs
(Help) (use ScanProsite for more details about PROSITE matches)


Matches on query sequence
Mat
Submission
1
50
100
1
THIO_HELPY
Q7MSG6
Q9PIY0
Q7VK37
Q9RVS8
Q8EPI6
THIO_STAEP
THIO_STAAM
THIO_BACSU
Q7MXW5
Q6GHU0
Q6GA69
THI2_CHLTE
Q9KWL9
Q9K8A8
THIO_CYACA
Q72B01
Q7VBF6
THI1_ANASP
Q8DKP7
THIO_HAEIN
Q6LLL6
Q8ZAD9
Q8A5L0
THIO_PSEAE
THIO_ECOLI
Q9KV51
Q9RYY9
THIM_PEA
Q87KH6
Q9CF37
Q7VKR2
Q7NM87
THIO_PORYE
THIM_ORYSA
Q97EM7
Q7V6M6
THIO_PORPU
THIM_WHEAT
Q6CZE0
Q7CET1
Q99Y75
Q8NZI7
Q8E3J7
Q8DXX8
Q879K6
Q7NXP2
THIO_SYNY3
THI1_SYNP7
THI1_CORNE
Q8YVV7
Q8DDN7
Q7MGP8
O67747
O28984
Q7V126
Q7UJ35
Q7MYL3
Q7U898
Q95AH9
THIO_LISMO
Q720J6
Q8YE56
Q8FXY9
Q835H2
THIO_STRAU
Q6G588
THIM_SPIOL
THIM_MAIZE
Q81L73
Q817L8
Q72ZM0
Q6HD04
Q8EJQ6
Q8DSD2
Q8L1N0
Q8P4D3
Q7M0Y9
Q88CG6
Q83A24
Q72HU9
Q8UJA6
Q97P68
Q7D2B9
THIO_RICCN
Q8DNP9

Alignments

sp P56430 THIO_HELPY **Thioredoxin (TRX) [trxA] [Helicobacter pylori (Campylobacter pylori), Helicobacter pylori J99 (Campylobacter pylori J99)]** 106 AA align

Score = 216 bits (551), Expect = 5e-56
Identities = 106/106 (100%), Positives = 106/106 (100%)

```
Query: 1   MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE
Sbjct: 1   MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
           QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG
Sbjct: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
```

tr Q7MSG6 **THIOREDOXIN [TRXA] [Wolinella succinogenes]** 106 AA align

Score = 157 bits (396), Expect = 4e-38
Identities = 67/106 (63%), Positives = 89/106 (83%)

```
Query: 1   MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           M  YIEL   NF+   KKGV+LVDFWAPWCGPC+M++PVI+ELA+++EGKA +CKVNTDE
Sbjct: 1   MGKYIELNASNFDEVTKKGVSLVDFWAPWCGPCRMVAPVIEELAADFEGKANVCKVNTDE 60

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
           ++EL+ K+GIRSIPT+LF KDGE+V Q++G  +K A KE+L+ L+G
Sbjct: 61  EQELAVKYGIRSIPTILFFKDGEIVDQMIGASSKQAFKEKLDSLIG 106
```

tr Q9PIY0 **Thioredoxin [trxA] [Campylobacter jejuni]** 104 AA align

Score = 155 bits (393), Expect = 1e-37
Identities = 72/105 (68%), Positives = 91/105 (86%), Gaps = 1/105 (0%)

```
Query: 1   MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           M  YIELT +NF    K+GVALVDFWAPWCGPC+ML+PVIDEL+++++GKAKICKVNTDE
Sbjct: 1   MGKYIELTSDNFAQA-KEGVALVDFWAPWCGPCRMLAPVIDELSNDFDGKAKICKVNTDE 59

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           Q +L+A+FG+RSIPTL+F K+GEVV QLVG Q+K A+ ++LN LL
Sbjct: 60  QGDLAAEFGVRSIPTLIFFKNGEVVDQLVGAQSKQAISDKLNSLL 104
```

tr Q7VK37 **Thioredoxin [trxA_2] [Helicobacter hepaticus]** 105 AA align

```
 Score =  146 bits (368), Expect = 8e-35
 Identities = 66/105 (62%), Positives = 83/105 (78%)

Query: 1   MSHYIELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           M+ Y ELT +NF++    GVALVDFWAPWC PCKMLSPVID+LA EYEGKAKICKVN DE
Sbjct: 1   MAKYKELTNDNFDTEALSGVALVDFWAPWCNPCKMLSPVIDKLADEYEGKAKICKVNVDE 60

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           Q ELS +FGIR+IPT+LF KDGE+  Q+ G   +  ++++L+ +L
Sbjct: 61  QGELSKRFGIRNIPTILFMKDGEIKDQVTGAMPEQVIRQKLDSIL 105
```

tr Q9RVS8 **Thioredoxin [DR0944] [Deinococcus radiodurans]** 141 AA
align

```
 Score =  120 bits (302), Expect = 3e-27
 Identities = 53/102 (51%), Positives = 74/102 (71%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +ELT+ NF S I +G+ LVDFWAPWCGPC++++PVI+ELA +YEG+ K+ KVN D+
Sbjct: 36  VELTDGNFTSEIAQGLTLVDFWAPWCGPCRIIAPVIEELAGQYEGRVKVAKVNVDDNPAT 95

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
           S +F + SIPT++  KDG+ V  +VG Q K A +  L+K LG
Sbjct: 96  SGQFRVMSIPTMILFKDGQPVEGMVGAQPKRAFESVLDKHLG 137
```

tr Q8EPI6 **Thioredoxin [OB2117] [Oceanobacillus iheyensis]** 104 AA
align

```
 Score =  119 bits (299), Expect = 8e-27
 Identities = 51/97 (52%), Positives = 72/97 (73%)

Query: 7   LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           +T++NF      KG+ L DFWAPWCGPCKM++PV++E+  E E K +I K++ DE +E +
Sbjct: 6   VTDQNFTEETSKGLVLADFWAPWCGPCKMIAPVLEEIDGEMEEKVQIVKLDVDENQETAG 65

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           KFG+ SIPTLL  KDG+VV Q++G Q K AL++ +NK
Sbjct: 66  KFGVMSIPTLLLFKDGDVVDQVIGFQPKEALEDLINK 102
```

sp Q8CPL5 THIO_STAEP **Thioredoxin (TRX) [trxA] [Staphylococcus epidermidis]** 104 AA
align

```
 Score =  116 bits (291), Expect = 7e-26
 Identities = 53/101 (52%), Positives = 75/101 (73%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +++T+ +F+S I+ GV LVDFWA WCGPCKM++PV++ELA +Y+GKA I K++ DE
Sbjct: 4   VKVTDSDFDSKIESGVKLVDFWATWCGPCKMIAPVLEELAGDYDGKADILKLDVDENPST 63
```

```
Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +AK+ + SIPTL+  KDGE V ++VG Q K  L E L+K L
Sbjct: 64  AAKYEVMSIPTLIVFKDGEPVDKVVGFQPKENLAEVLDKHL 104
```

sp Q9ZEH4 THIO_STAAM **Thioredoxin (TRX) [trxA] [Staphylococcus aureus (strain Mu50 / ATCC 700699), Staphylococcus aureus (strain N315), Staphylococcus aureus (strain MW2), Staphylococcus aureus]** 104 AA align

```
 Score =  116 bits (290), Expect = 9e-26
 Identities = 52/101 (51%), Positives = 76/101 (74%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +++T+ +F+S ++ GV LVDFWA WCGPCKM++PV++ELA++YEGKA I K++ DE
Sbjct: 4   VKVTDADFDSKVESGVQLVDFWATWCGPCKMIAPVLEELAADYEGKADILKLDVDENPST 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +AK+ + SIPTL+  KDG+ V ++VG Q K  L E L+K L
Sbjct: 64  AAKYEVMSIPTLIVFKDGQPVDKVVGFQPKENLAEVLDKHL 104
```

sp P14949 THIO_BACSU **Thioredoxin (TRX) [trxA] [Bacillus subtilis]** 103 AA align

```
 Score =  116 bits (290), Expect = 9e-26
 Identities = 52/101 (51%), Positives = 72/101 (70%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           ++ T+++F +   +GV L DFWAPWCGPCKM++PV++EL  E   K KI K++ DE +E
Sbjct: 3   VKATDQSFSAETSEGVVLADFWAPWCGPCKMIAPVLEELDQEMGDKLKIVKIDVDENQET 62

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           + K+G+ SIPTLL  KDGEVV   VG + K AL+E +NK L
Sbjct: 63  AGKYGVMSIPTLLVLKDGEVVETSVGFKPKEALQELVNKHL 103
```

tr Q7MXW5 **Thioredoxin [trx] [Porphyromonas gingivalis (Bacteroides gingivalis)]** 104 AA align

```
 Score =  116 bits (290), Expect = 9e-26
 Identities = 52/101 (51%), Positives = 76/101 (74%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALV-DFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           +++T+  F+  + +G  +V DFWA WCGPC+M+ P+IDELA+EYEG+A I KV+ D  E
Sbjct: 3   LQITDATFDGLVAEGKPMVVDFWATWCGPCRMVGPIIDELAAEYEGRAIIGKVDVDANTE 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
           L  K+G+R+IPT+LF K+GEVV +LVG Q+K   K++L+ L
Sbjct: 63  LPMKYGVRNIPTILFIKNGEVVKKLVGAQSKDVFKKELDAL 103
```

tr Q6GHU0 **Thioredoxin [trxA] [Staphylococcus aureus subsp. aureus MRSA252]** 104 AA align

Score = 116 bits (290), Expect = 9e-26
Identities = 52/101 (51%), Positives = 76/101 (74%)

```
Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +++T+ +F+S ++ GV LVDFWA WCGPCKM++PV++ELA++YEGKA I K++ DE
Sbjct: 4   VKVTDADFDSKVESGVQLVDFWATWCGPCKMIAPVLEELAADYEGKADILKLDVDENPST 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +AK+ + SIPTL+  KDG+ V ++VG Q K  L E L+K L
Sbjct: 64  AAKYEVMSIPTLIVFKDGQPVDKVVGFQPKENLAEVLDKHL 104
```

tr Q6GA69 **Thioredoxin [SAS1079] [Staphylococcus aureus subsp. aureus MSSA476]** 104 AA align

Score = 116 bits (290), Expect = 9e-26
Identities = 52/101 (51%), Positives = 76/101 (74%)

```
Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +++T+ +F+S ++ GV LVDFWA WCGPCKM++PV++ELA++YEGKA I K++ DE
Sbjct: 4   VKVTDADFDSKVESGVQLVDFWATWCGPCKMIAPVLEELAADYEGKADILKLDVDENPST 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +AK+ + SIPTL+  KDG+ V ++VG Q K  L E L+K L
Sbjct: 64  AAKYEVMSIPTLIVFKDGQPVDKVVGFQPKENLAEVLDKHL 104
```

sp Q8KE49 THI2_CHLTE **Thioredoxin 2 (Trx-2) [trx2] [Chlorobium tepidum]** 108 AA align

Score = 115 bits (288), Expect = 1e-25
Identities = 55/105 (52%), Positives = 74/105 (70%), Gaps = 2/105 (1%)

```
Query: 4   YIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQ 61
           Y E T++NF++ I     VALVDFWA WCGPC ML PVI+ELA +YEGKA I K+N DE
Sbjct: 4   YFEATDQNFQAEILNSDKVALVDFWAAWCGPCMMLGPVIEELAGDYEGKAIIAKLNVDEN 63

Query: 62  EELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
              + ++GIRSIPT+L  K G+VV Q+VG    K  + ++L++ +G
Sbjct: 64  PNTAGQYGIRSIPTMLIIKGGKVVDQMVGALPKNMIAKKLDEHIG 108
```

tr Q9KWL9 **Thioredoxin [Staphylococcus warneri]** 104 AA align

Score = 115 bits (288), Expect = 1e-25
Identities = 56/101 (55%), Positives = 73/101 (71%)

```
Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           I +TE+ F  TI+KGV LVDFWA WC PC+M SPV++EL+ E EGK  I KV+ DE++ L
Sbjct: 4   ITVTEKTFNKTIEKGVTLVDFWATWCPPCQMQSPVLEELSDELEGKVIIGKVDVDEEKAL 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +AK+ I+SIPTLL  KDGE+V+ L+G   K  L+  L K L
Sbjct: 64  AAKYQIQSIPTLLIFKDGELVNTLIGFNPKPNLENVLTKYL 104
```

tr Q9K8A8 **Thioredoxin [trxA] [Bacillus halodurans]** 104 AA align

```
 Score =  114 bits (285), Expect = 3e-25
 Identities = 51/101 (50%), Positives = 70/101 (68%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           + +T++ F     +G+ L DFWAPWCGPCKM++PV++EL  E   K KI K++ DE +E
Sbjct: 4   VNVTDQTFAQETSEGLVLADFWAPWCGPCKMIAPVLEELDGEMGDKVKIAKLDVDENQET 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           ++KF + SIPTL+  KDG+VV Q+ G Q K AL E LNK L
Sbjct: 64  ASKFNVMSIPTLIVFKDGQVVDQVTGFQPKDALAELLNKHL 104
```

sp P37395 THIO_CYACA **Thioredoxin [trxA] [Cyanidium caldarium]** 107 AA align

```
 Score =  113 bits (283), Expect = 6e-25
 Identities = 54/103 (52%), Positives = 72/103 (69%), Gaps = 2/103 (1%)

Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I++T+ +FE  +   + + LVDFWAPWCGPC+M+SPVIDELA EY  + KI K+NTDE
Sbjct: 5   IQVTDFSFEKEVVNSEKLVLVDFWAPWCGPCRMISPVIDELAQEYVEQVKIVKINTDENP 64

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
            +SA++GIRSIPTL+  KDG+ V  ++G   K  L   L K L
Sbjct: 65  SISAEYGIRSIPTLMLFKDGKRVDTVIGAVPKSTLTNALKKYL 107
```

tr Q72B01 **Thioredoxin [trx] [Desulfovibrio vulgaris (strain Hildenborough / ATCC 29579 / NCIMB 8303)]** 107 AA align

```
 Score =  112 bits (280), Expect = 1e-24
 Identities = 51/104 (49%), Positives = 74/104 (71%), Gaps = 3/104 (2%)

Query: 6   ELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           ++T+  FE+++ K     L+DFWAPWCGPC+ + PVIDELA+EYEGK  I K+N D+
Sbjct: 4   QITDATFEASVLKSAIPVLIDFWAPWCGPCRAMGPVIDELAAEYEGKVLIVKMNVDDNPA 63

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQL-NKLLG 106
             +K+GIR+IPTL+  K+GEVV Q+ G  +K ++K ++ + K LG
```

```
Sbjct: 64  TPSKYGIRAIPTLILFKNGEVVEQVTGAVSKSSIKDMIAQKALG 107
```

tr Q7VBF6 **Thioredoxin family protein [trxA] [Prochlorococcus marinus]** 107 AA

align

```
 Score =  111 bits (278), Expect = 2e-24
 Identities = 49/107 (45%), Positives = 74/107 (68%), Gaps = 2/107 (1%)

Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS    +T+ +FE  + +     LVDFWAPWCGPC+M+SP++DE++ ++EGK K+CK+NT
Sbjct: 1   MSSAAAVTDSSFEQEVLQSDLPVLVDFWAPWCGPCRMVSPIVDEISKDFEGKIKVCKLNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           DE   +++++GIRSIPTL+  K G+ V  +VG   K  L   ++K L
Sbjct: 61  DENPNVASQYGIRSIPTLMIFKGGQKVDTVVGAVPKATLSGTISKHL 107
```

sp P06544 THI1_ANASP **Thioredoxin 1 (TRX-1) (Thioredoxin M) [trxA] [Anabaena sp. (strain PCC 7120), Anabaena sp. (strain PCC 7119)]** 106 AA align

```
 Score =  110 bits (276), Expect = 4e-24
 Identities = 51/99 (51%), Positives = 70/99 (70%), Gaps = 6/99 (6%)

Query: 13  ESTIKKGV------ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           +ST K+ V       LVDFWAPWCGPC+M++PV+DE+A +YEGK K+ KVNTDE  ++++
Sbjct: 8   DSTFKQEVLDSDVPVLVDFWAPWCGPCRMVAPVVDEIAQQYEGKIKVVKVNTDENPQVAS 67

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           ++GIRSIPTL+  K G+ V  +VG   K  L + L K L
Sbjct: 68  QYGIRSIPTLMIFKGGQKVDMVVGAVPKTTLSQTLEKHL 106
```

tr Q8DKP7 **Thioredoxin [tll0812] [Synechococcus elongatus (Thermosynechococcus elongatus)]** 107 AA align

```
 Score =  110 bits (276), Expect = 4e-24
 Identities = 51/107 (47%), Positives = 72/107 (66%), Gaps = 2/107 (1%)

Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS  + +T+  FE  +       LVDFWAPWCGPC+M++PV+DE+A+EY+G+ K+ KVNT
Sbjct: 1   MSSALSVTDATFEEEVLNSDIPVLVDFWAPWCGPCRMVAPVVDEIANEYQGRVKVVKVNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           DE  +++  FGIRSIPTL+  K G+ V  LVG   K  ++  L + L
Sbjct: 61  DENSKVATDFGIRSIPTLMIFKGGQKVDILVGAVPKTKIEATLAQFL 107
```

sp P43785 THIO_HAEIN **Thioredoxin (TRX) [trxA] [Haemophilus influenzae]** 107 AA align

```
 Score =  109 bits (273), Expect = 8e-24
 Identities = 51/105 (48%), Positives = 70/105 (66%), Gaps = 2/105 (1%)

Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS  + + + +FES +       L+DFWAPWCGPCKM++PV+DELA E+ GK KI K+N
Sbjct: 1   MSEVLHINDADFESVVVNSDIPILLDFWAPWCGPCKMIAPVLDELAPEFAGKVKIVKMNV 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           D+ +   A+FG+RSIPTLL  K+G+VV   VG   K  L   +N+
Sbjct: 61  DDNQATPAQFGVRSIPTLLLIKNGQVVATQVGALPKTQLANFINQ 105
```

tr Q6LLL6 **Putative thioredoxin [SO0406] [Photobacterium profundum (Photobacterium sp. (strain SS9))]** 112 AA align

```
 Score =  109 bits (272), Expect = 1e-23
 Identities = 52/100 (52%), Positives = 67/100 (67%), Gaps = 2/100 (2%)

Query: 5   IELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           ++LT+  F+S +    G  LVDFWA WCGPCKM++P++DE+A+EYEGK  I K+N D+
Sbjct: 10  VQLTDATFDSDVVNAAGPVLVDFWAEWCGPCKMIAPILDEIANEYEGKVTIGKLNIDQNA 69

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
              KFGIR IPTLL  KDG V    VG  +K  LKE L+
Sbjct: 70  ATPPKFGIRGIPTLLLFKDGSVAATKVGALSKTQLKEFLD 109
```

tr Q8ZAD9 **Thioredoxin 1 [trxA] [Yersinia pestis]** 108 AA align

```
 Score =  109 bits (272), Expect = 1e-23
 Identities = 50/100 (50%), Positives = 72/100 (72%), Gaps = 2/100 (2%)

Query: 5   IELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I L++++F++ + K  G+ LVDFWA WCGPCKM++P++DE+A EYEG+  I K+N D+ +
Sbjct: 6   IHLSDDSFDTDVLKASGLVLVDFWAEWCGPCKMIAPILDEIAEEYEGRLTIAKLNIDDNQ 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
             + K+GIR IPTLL  +DGEVV   VG  +K  LK  L+
Sbjct: 66  GTAPKYGIRGIPTLLLFRDGEVVATKVGALSKGQLKAFLD 105
```

tr Q8A5L0 **Thioredoxin (Thioredoxin M) [BT2229] [Bacteroides thetaiotaomicron]** 104 AA align

```
 Score =  109 bits (272), Expect = 1e-23
 Identities = 47/102 (46%), Positives = 76/102 (74%), Gaps = 1/102 (0%)
```

```
Query: 5   IELTEENFESTIKKGV-ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           +E+T+ N++  + +G   +VDFWAPWCGPCKM++P+I+ELA+E+EG+  I K + D+  +
Sbjct: 3   LEITDSNYKEILAEGKPVVVDFWAPWCGPCKMVAPIIEELAAEFEGQVIIGKCDVDDNSD 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           ++A++GIR+IPT+LF K+GE+V + VG   K    E++  LL
Sbjct: 63  VAAEYGIRNIPTVLFFKNGEIVDKQVGAVAKPVFVEKVKNLL 104
```

sp Q9X2T1 THIO_PSEAE **Thioredoxin (TRX) [trxA] [Pseudomonas aeruginosa]** 108 AA align

```
 Score =  108 bits (271), Expect = 1e-23
 Identities = 47/97 (48%), Positives = 67/97 (68%), Gaps = 2/97 (2%)

Query: 3   HYIELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           H + +T+ +FE  + K  G  LVD+WA WCGPCKM++PV+DE+A +Y+GK K+CK+N DE
Sbjct: 4   HIVNVTDASFEQDVLKADGPVLVDYWAEWCGPCKMIAPVLDEVARDYQGKLKVCKLNIDE 63

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
            ++   K+G+R IPTL+  KDG V    VG  +K  L
Sbjct: 64  NQDTPPKYGVRGIPTLMLFKDGNVEATKVGALSKSQL 100
```

sp P00274 THIO_ECOLI **Thioredoxin 1 (TRX1) (TRX) [trxA] [Escherichia coli, Escherichia coli O6, Escherichia coli O157:H7, Salmonella typhimurium, Salmonella typhi, Shigella flexneri]** 108 AA align

```
 Score =  108 bits (270), Expect = 2e-23
 Identities = 50/100 (50%), Positives = 70/100 (70%), Gaps = 2/100 (2%)

Query: 5   IELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I LT+++F++ + K  G  LVDFWA WCGPCKM++P++DE+A EY+GK  + K+N D+
Sbjct: 5   IHLTDDSFDTDVLKADGAILVDFWAEWCGPCKMIAPILDEIADEYQGKLTVAKLNIDQNP 64

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
             + K+GIR IPTLL  K+GEV    VG  +K  LKE L+
Sbjct: 65  GTAPKYGIRGIPTLLLFKNGEVAATKVGALSKGQLKEFLD 104
```

tr Q9KV51 **Thioredoxin [VC0306] [Vibrio cholerae]** 108 AA align

```
 Score =  108 bits (270), Expect = 2e-23
 Identities = 53/100 (53%), Positives = 67/100 (67%), Gaps = 2/100 (2%)

Query: 5   IELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           ++LT++ FE+ + K  G  LVDFWA WCGPCKM++P++DE+A EY GK  I K+N D
Sbjct: 6   LQLTDDGFENDVIKAAGPVLVDFWAEWCGPCKMIAPILDEVADEYAGKLTIGKLNIDHNA 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
               KFGIR IPTLL  KDG VV   VG  +K  LKE L+
```

```
Sbjct: 66  GTPPKFGIRGIPTLLLFKDGSVVATKVGALSKTQLKEFLD 105
```

tr Q9RYY9 **Thioredoxin 1 [DRA0164] [Deinococcus radiodurans]** 142 AA align

```
 Score =  108 bits (270), Expect = 2e-23
 Identities = 52/101 (51%), Positives = 70/101 (68%), Gaps = 4/101 (3%)

Query: 8   TEENFESTIKKGV-ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           T+  FE  ++  V  LVDFWAPWCGPC+++ PV+++LA +  GK ++ KVN DE    +A
Sbjct: 41  TDATFEQDLQTSVPVLVDFWAPWCGPCRVMGPVLEDLARDLPGKVRVVKVNVDENPRTAA 100

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALK---EQLNKL 104
           +F +RSIPTLL  KDGE V Q+VGV  K AL+   E LN+L
Sbjct: 101 RFEVRSIPTLLMFKDGEEVDQMVGVTQKAALRARVEHLNQL 141
```

sp P48384 THIM_PEA **Thioredoxin M-type, chloroplast precursor (TRX-M) [Pisum sativum (Garden pea)]** 172 AA align

```
 Score =  108 bits (269), Expect = 2e-23
 Identities = 47/84 (55%), Positives = 61/84 (71%)

Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           LVDFWAPWCGPC+M++P+IDELA EY GK K  K+NTDE    + K+GIRSIPT+LF K+
Sbjct: 89  LVDFWAPWCGPCRMIAPIIDELAKEYAGKIKCYKLNTDESPNTATKYGIRSIPTVLFFKN 148

Query: 82  GEVVHQLVGVQTKVALKEQLNKLL 105
           GE    ++G   K  L E++ K +
Sbjct: 149 GERKDSVIGAVPKATLSEKVEKYI 172
```

tr Q87KH6 **Thioredoxin [VP3001] [Vibrio parahaemolyticus]** 108 AA align

```
 Score =  108 bits (269), Expect = 2e-23
 Identities = 52/100 (52%), Positives = 66/100 (66%), Gaps = 2/100 (2%)

Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           ++LT++ FE+ +    G  LVDFWA WCGPCKM++P++DE+A EYEGK  I K+N D
Sbjct: 6   LQLTDDGFENDVINAAGPVLVDFWAEWCGPCKMIAPILDEIAEEYEGKLTIGKLNIDHNA 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
              KFGIR IPTLL  KDG V    VG  +K  LKE L+
Sbjct: 66  GTPPKFGIRGIPTLLLFKDGNVAATKVGALSKTQLKEFLD 105
```

tr Q9CF37 **Thioredoxin [trxA] [Lactococcus lactis (subsp. lactis)]** 104 AA align

(Streptococcus lactis)]

Score = 107 bits (268), Expect = 3e-23
Identities = 48/99 (48%), Positives = 70/99 (70%), Gaps = 1/99 (1%)

```
Query: 7   LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEELS 65
           +T+  F+   K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KICK++ DE    +
Sbjct: 5   ITDATFDEETKEGLVLIDFWATWCGPCRMQAPILEQLSEELDESELKICKMDVDENPATA 64

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
             FGI SIPTL+F KDGE V ++VGVQTK  LK  + +L
Sbjct: 65  QGFGIMSIPTLMFKKDGEEVKRIVGVQTKAQLKAVIAEL 103
```

tr Q7VKR2 **Thioredoxin [trxA] [Haemophilus ducreyi]** 105 AA
align

Score = 107 bits (268), Expect = 3e-23
Identities = 52/99 (52%), Positives = 71/99 (71%), Gaps = 4/99 (4%)

```
Query: 1  MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
          M+H  ++T+  FE  + K     L+DFWAPWCGPC+ ++P +DELA E+ G+AK+ KVN
Sbjct: 1  MTH--QVTDATFEQEVLKSDLPVLLDFWAPWCGPCRTIAPWLDELAQEFAGRAKVAKVNV 58

Query: 59 DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
          DE ++++A+FGIRSIPTLL  K+GEVV   VGV  K  L
Sbjct: 59 DENQQIAAQFGIRSIPTLLLFKNGEVVAIQVGVLPKSQL 97
```

tr Q7NM87 **Thioredoxin [gll0880] [Gloeobacter violaceus]** 110 AA
align

Score = 107 bits (268), Expect = 3e-23
Identities = 49/105 (46%), Positives = 70/105 (66%), Gaps = 2/105 (1%)

```
Query: 1   MSHYIELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS  + + + NF++ +       LVDFWAPWCGPC+M++PV+DE+A +Y GK K+ KVNT
Sbjct: 1   MSAAVPVGDSNFKTEVLDSELPVLVDFWAPWCGPCRMVAPVVDEIAQQYSGKLKVVKVNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           DE  ++++++GIRSIPTL+  K G  V  +VG   K  L   L K
Sbjct: 61  DENPQVASQYGIRSIPTLMVFKSGSKVDMVVGAVPKTTLATTLEK 105
```

sp P50254 THIO_PORYE **Thioredoxin [trxA] [Porphyra yezoensis]** 107 AA
align

Score = 107 bits (267), Expect = 4e-23
Identities = 48/102 (47%), Positives = 69/102 (67%), Gaps = 2/102 (1%)

```
Query: 6   ELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           ++T+ +F+  +       LVDFWAPWCGPC+M+SPV+DE+AEEYESSIKVVKINTDDNPT
Sbjct: 5   QVTDASFKQEVINNNLPVLVDFWAPWCGPCRMVSPVVDEIAEEYESSIKVVKINTDDNPT 64
```

```
Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           ++A++GIRSIPTL+  K GE V  ++G   K  L   LNK +
Sbjct: 65  IAAEYGIRSIPTLMIFKAGERVDTVIGAVPKSTLASTLNKYI 106
```

sp Q9ZP20 THIM_ORYSA **Thioredoxin M-type, chloroplast precursor (TRX-M) [Oryza sativa (Rice)]** 172 AA align

```
 Score =  107 bits (267), Expect = 4e-23
 Identities = 48/97 (49%), Positives = 67/97 (68%), Gaps = 2/97 (2%)

Query: 9   EENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           E+N++S +   +   LV+FWAPWCGPC+M++PVIDELA EY GK K CKVNTD+   ++
Sbjct: 72  EKNWDSMVLGSEAPVLVEFWAPWCGPCRMIAPVIDELAKEYVGKIKCCKVNTDDSPNIAT 131

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
            +GIRSIPT+L  K+GE    ++G   K  L   ++K
Sbjct: 132 NYGIRSIPTVLMFKNGEKKESVIGAVPKTTLATIIDK 168
```

tr Q97EM7 **Thioredoxin [CAC3083] [Clostridium acetobutylicum]** 105 AA align

```
 Score =  107 bits (267), Expect = 4e-23
 Identities = 50/100 (50%), Positives = 66/100 (66%), Gaps = 2/100 (2%)

Query: 6   ELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           E+ E  F+  IK      +VDFWAPWCGPCKML P+IDEL+ + +GKAK  KVN DE
Sbjct: 4   EINESIFDEEIKTSGEPVIVDFWAPWCGPCKMLGPIIDELSEDLDGKAKFTKVNVDENPG 63

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           +++KFGI SIPT++  KDG  V  LVG + K ++   + K
Sbjct: 64  IASKFGIASIPTVMIFKDGNPVETLVGFRPKQSITASIEK 103
```

tr Q7V6M6 **Thioredoxin [trxA] [Prochlorococcus marinus (strain MIT 9313)]** 107 AA align

```
 Score =  107 bits (266), Expect = 5e-23
 Identities = 48/107 (44%), Positives = 73/107 (67%), Gaps = 2/107 (1%)

Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS+   +T+ +FE  + +     LVDFWAPWCGPC+M++P++DE+A E+E K K+ K+NT
Sbjct: 1   MSNAAAVTDASFEQDVLQSDVPVLVDFWAPWCGPCRMVAPIVDEIAKEFESKIKVFKLNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           DE   +++++GIRSIPTL+  K G+ V  +VG   K  L   ++K L
Sbjct: 61  DENPNVASQYGIRSIPTLMVFKGGQKVDTVVGAVPKATLSGTISKYL 107
```

sp Q9ZP21 THIM_WHEAT **Thioredoxin M-type, chloroplast precursor (TRX-M) [Triticum aestivum (Wheat)]** 175 AA align

Score = 106 bits (265), Expect = 7e-23
Identities = 48/100 (48%), Positives = 70/100 (70%), Gaps = 2/100 (2%)

```
Query: 9   EENFESTIK--KGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           E+N+++ +   +   LV+FWAPWCGPC+M++PVIDELA +Y GK K CKVNTD+   +++
Sbjct: 75  EKNWDNMVIACESPVLVEFWAPWCGPCRMIAPVIDELAKDYVGKIKCCKVNTDDCPNIAS 134

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLLG 106
            +GIRSIPT+L  KDGE    ++G   K  L   ++K +G
Sbjct: 135 TYGIRSIPTVLMFKDGEKKESVIGAVPKTTLCTIIDKYIG 174
```

tr Q6CZE0 **Thioredoxin [ECA4212] [Erwinia carotovora subsp. atroseptica SCRI1043]** 108 AA align

Score = 106 bits (265), Expect = 7e-23
Identities = 50/99 (50%), Positives = 68/99 (68%), Gaps = 2/99 (2%)

```
Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I LT+++F + +   +G  LVDFWA WCGPCKM++P++DE+A E+EGK  + K+N DE
Sbjct: 6   IHLTDDSFGTKVLQAEGATLVDFWAEWCGPCKMIAPILDEIAEEFEGKLTVTKLNIDENP 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQL 101
             + K+GIR IPTLL  K+GEV    VG  +K  LKE L
Sbjct: 66  ATAPKYGIRGIPTLLLFKNGEVAATKVGALSKGQLKEFL 104
```

tr Q7CET1 **Putative thioredoxin [trx.2] [Streptococcus pyogenes (serotype M3)]** 104 AA align

Score = 106 bits (264), Expect = 9e-23
Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

```
Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 3   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQAPILEQLSQEIDEDELKILKMDVDENPE 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
            + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 63  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 103
```

tr Q99Y75 **Putative thioredoxin [trx] [Streptococcus pyogenes]** 104 AA align

Score = 106 bits (264), Expect = 9e-23

```
 Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 3   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQAPILEQLSQEIDEDELKILKMDVDENPE 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
            + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 63  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 103
```

tr Q8NZI7 **Putative thioredoxin [trxA] [Streptococcus pyogenes (serotype M18)]** 104 AA align

```
 Score =  106 bits (264), Expect = 9e-23
 Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 3   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQTPILEQLSQEIDEDELKILKMDVDENPE 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
            + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 63  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 103
```

tr Q8E3J7 **Hypothetical protein gbs1762 [gbs1762] [Streptococcus agalactiae (serotype III)]** 104 AA align

```
 Score =  106 bits (264), Expect = 9e-23
 Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 3   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQAPILEQLSQEIDEDELKILKMDVDENPE 62

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
            + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 63  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 103
```

tr Q8DXX8 **Thioredoxin [trx] [Streptococcus agalactiae (serotype V)]** 104 AA align

```
 Score =  106 bits (264), Expect = 9e-23
 Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 3   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQAPILEQLSQEIDEDELKILKMDVDENPE 62
```

```
Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
           + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 63  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 103
```

tr Q879K6 **Putative thioredoxin [SPs0281] [Streptococcus pyogenes (serotype M3)]** 110 AA align

```
 Score =  106 bits (264), Expect = 9e-23
 Identities = 49/101 (48%), Positives = 71/101 (69%), Gaps = 1/101 (0%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEE 63
           +E+T+  F    K+G+ L+DFWA WCGPC+M +P++++L+ E  E + KI K++ DE  E
Sbjct: 9   LEVTDATFVEETKEGLVLIDFWATWCGPCRMQAPILEQLSQEIDEDELKILKMDVDENPE 68

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
           + +FGI SIPTL+F KDGEVV Q+ GV TK  LK  + +L
Sbjct: 69  TARQFGIMSIPTLMFKKDGEVVKQVAGVHTKDQLKAIIAEL 109
```

tr Q7NXP2 **Thioredoxin [trxA] [Chromobacterium violaceum]** 108 AA align

```
 Score =  106 bits (264), Expect = 9e-23
 Identities = 47/95 (49%), Positives = 67/95 (70%), Gaps = 2/95 (2%)

Query: 5   IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           + +T+++FE+ + K     LVD+WA WCGPCKM++P++DE+A EY+GK KI K+N D+ E
Sbjct: 6   LHVTDDSFENEVLKADRPVLVDYWAEWCGPCKMIAPILDEVAKEYDGKLKIAKLNIDQNE 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
           +   KFGIR IPTL+  KDG+V    VG  +K  L
Sbjct: 66  QTPPKFGIRGIPTLMLFKDGQVAATKVGALSKSQL 100
```

sp P52231 THIO_SYNY3 **Thioredoxin (TRX) [trxA] [Synechocystis sp. (strain PCC 6803)]** 106 AA align

```
 Score =  105 bits (263), Expect = 1e-22
 Identities = 45/84 (53%), Positives = 61/84 (72%)

Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           LVDFWAPWCGPC+M++PV+DE++ +YEGK K+ K+NTDE    ++++GIRSIPTL+  K
Sbjct: 23  LVDFWAPWCGPCRMVAPVVDEISQQYEGKVKVVKLNTDENPNTASQYGIRSIPTLMIFKG 82

Query: 82  GEVVHQLVGVQTKVALKEQLNKLL 105
           G+ V  +VG   K  L   L K L
Sbjct: 83  GQRVDMVVGAVPKTTLASTLEKYL 106
```

sp P00275 THI1_CORNE **Thioredoxin C-1 [Corynebacterium nephridii]** 105 AA align

Score = 105 bits (263), Expect = 1e-22
Identities = 48/97 (49%), Positives = 67/97 (68%), Gaps = 2/97 (2%)

```
Query: 5  IELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
          +++   NF+S + +      +VDFWA WCGPCKM++P +DE+A+E  G+ KI KVN DE
Sbjct: 3  VKVDNSNFQSDVLQSSEPVVVDFWAEWCGPCKMIAPALDEIATEMAGQVKIAKVNIDENP 62

Query: 63 ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKE 99
          EL+A+FG+RSIPTLL  KDGE+   +VG   K  L +
Sbjct: 63 ELAAQFGVRSIPTLLMFKDGELAANMVGAAPKSRLAD 99
```

tr Q8YVV7 **Thioredoxin [all1866] [Anabaena sp. (strain PCC 7120)]** 110 AA align

Score = 105 bits (263), Expect = 1e-22
Identities = 49/105 (46%), Positives = 70/105 (66%), Gaps = 2/105 (1%)

```
Query: 1  MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
          MS    +TE  F+  +       LVDFWAPWCGPC+M++PV+DE+ASEYEG  K+ K+NT
Sbjct: 1  MSSITNVTEATFKQEVLDSNVPVLVDFWAPWCGPCRMVAPVVDEVASEYEGLVKVVKLNT 60

Query: 59 DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
          D+   +++ +GIRSIPTL+  K G  V+ +VG   +K  L + L +
Sbjct: 61 DQNPTVASHYGIRSIPTLMVFKGGRQVNTVVGAVSKTTLTKTLTQ 105
```

tr Q8DDN7 **Thioredoxin [VV10938] [Vibrio vulnificus]** 108 AA align

Score = 105 bits (263), Expect = 1e-22
Identities = 51/100 (51%), Positives = 66/100 (66%), Gaps = 2/100 (2%)

```
Query: 5  IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
          ++L++E FE+ +    G  LVDFWA WCGPCKM++P++DE+A EYEGK  I K+N D
Sbjct: 6  LQLSDEGFENDVINAAGPVLVDFWAEWCGPCKMIAPILDEIAEEYEGKLTIGKLNIDHNA 65

Query: 63 ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
              KFGIR IPTLL  K+G V     VG   +K  LKE L+
Sbjct: 66 GTPPKFGIRGIPTLLLFKNGSVAATKVGALSKTQLKEFLD 105
```

tr Q7MGP8 **Thiol-disulfide isomerase and thioredoxin [VV3182] [Vibrio vulnificus (strain YJ016)]** 112 AA align

Score = 105 bits (263), Expect = 1e-22
Identities = 51/100 (51%), Positives = 66/100 (66%), Gaps = 2/100 (2%)

```
Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           ++L++E FE+ +    G  LVDFWA WCGPCKM++P++DE+A EYEGK  I K+N D
Sbjct: 10  LQLSDEGFENDVINAAGPVLVDFWAEWCGPCKMIAPILDEIAEEYEGKLTIGKLNIDHNA 69

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
               KFGIR IPTLL  K+G V    VG  +K  LKE L+
Sbjct: 70  GTPPKFGIRGIPTLLLFKNGSVAATKVGALSKTQLKEFLD 109
```

tr O67747 **Thioredoxin [trxA1] [Aquifex aeolicus]** 139 AA align

```
 Score =  105 bits (263), Expect = 1e-22
 Identities = 49/101 (48%), Positives = 72/101 (70%), Gaps = 6/101 (5%)

Query: 5   IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           IEL E+N+E  + +     LVDFWAPWCGPC++++P+I+E+A E   K K+ K+NTDE
Sbjct: 6   IELNEQNWEQEVLQSDKPVLVDFWAPWCGPCRIIAPIIEEIAEELGDKVKVGKLNTDEN 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
            ++ ++GIR+IPT++  K+GEVV   +GVQ     KE+LNK
Sbjct: 66  NIAMRYGIRAIPTIILFKNGEVVDTRIGVQP----KERLNK 102
```

tr O28984 **Thioredoxin (Trx-3) [AF1284] [Archaeoglobus fulgidus]** 134 AA align

```
 Score =  105 bits (261), Expect = 2e-22
 Identities = 50/102 (49%), Positives = 68/102 (66%), Gaps = 1/102 (0%)

Query: 5   IELTEENFESTIKKGV-ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           ++L   NF+ T+K     +VDFWA WC PCKM++PVI+ELA EY GK    K+NTDE
Sbjct: 33  VKLNSSNFDETLKNNENVVVDFWAEWCMPCKMIAPVIEELAKEYAGKVVFGKLNTDENPT 92

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           ++A++GI +IPTL+F K G+ V QLVG   K  LK  + + L
Sbjct: 93  IAARYGISAIPTLIFFKKGKPVDQLVGAMPKSELKRWVQRNL 134
```

tr Q7V126 **Thioredoxin [trxA] [Prochlorococcus marinus subsp. pastoris (strain CCMP 1378 / MED4)]** 107 AA align

```
 Score =  104 bits (260), Expect = 3e-22
 Identities = 47/107 (43%), Positives = 73/107 (67%), Gaps = 2/107 (1%)

Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS    +T+ +F+  + +     LVDFWAPWCGPC+M++PV++E++ ++EGK K+ K+NT
Sbjct: 1   MSSAPAVTDSSFDKEVLQSNLPVLVDFWAPWCGPCRMVAPVVEEISKDFEGKIKVFKLNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           DE   +++++GIRSIPTL+  K G+ V  +VG   K  L   L+K L
Sbjct: 61  DENPNVASQYGIRSIPTLMIFKGGQKVDTVVGAVPKATLSSTLSKHL 107
```

tr Q7UJ35 **Thioredoxin 1 [trxA] [Rhodopirellula baltica]** 108 AA
align

Score = 104 bits (260), Expect = 3e-22
Identities = 52/101 (51%), Positives = 69/101 (67%), Gaps = 3/101 (2%)

```
Query: 6   ELTEENFESTIKKGVA--LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           E  ++NF+S + K  +  LVDFWAPWCGPC+ ++P+IDELASE  G  KI KVN D+
Sbjct: 8   EFNDDNFDSEVLKSDSPVLVDFWAPWCGPCRQIAPMIDELASENPG-VKIGKVNIDDNPG 66

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
            + KFGI SIPTLL  K+GE+    VGV+ K AL++ L  +
Sbjct: 67  AAQKFGINSIPTLLLFKNGEIADTFVGVRPKAALQDALTSV 107
```

tr Q7MYL3 **Thioredoxin 1 (TRX1) (TRX) [trxA] [Photorhabdus luminescens (subsp. laumondii)]** 108 AA
align

Score = 104 bits (260), Expect = 3e-22
Identities = 49/100 (49%), Positives = 67/100 (67%), Gaps = 2/100 (2%)

```
Query: 5   IELTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I L++ +F++ +    G  LVDFWA WCGPCKM++P++DE+A EY GK  I K+N D+
Sbjct: 6   IHLSDASFDTDVLNAAGPVLVDFWAAWCGPCKMIAPILDEIAPEYSGKLTITKLNIDDNP 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLN 102
             + K+GIR IPTLL  KDG+V    VG  +K  LKE L+
Sbjct: 66  ATAPKYGIRGIPTLLLFKDGQVAATKVGALSKTQLKEFLD 105
```

tr Q7U898 **Thioredoxin [trxA] [Synechococcus sp. (strain WH8102)]** 107 AA
align

Score = 104 bits (259), Expect = 3e-22
Identities = 46/107 (42%), Positives = 73/107 (67%), Gaps = 2/107 (1%)

```
Query: 1   MSHYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS    +T+ +FE  + +     LVDFWAPWCGPC+M++P+++E+A E++G+ K+ K+NT
Sbjct: 1   MSSAAAVTDASFEQDVLQSDVPVLVDFWAPWCGPCRMVAPIVEEIAKEFDGQIKVFKLNT 60

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           DE   +++++GIRSIPTL+  K G+ V  +VG   K  L   ++K L
Sbjct: 61  DENPNVASQYGIRSIPTLMVFKGGQKVDTVVGAVPKATLSGTISKYL 107
```

tr Q95AH9 **Putative thioredoxin m2 [trxm2] [Pisum sativum (Garden pea)]** 180 AA
align

```
 Score =  104 bits (259), Expect = 3e-22
 Identities = 48/101 (47%), Positives = 68/101 (66%), Gaps = 2/101 (1%)

Query: 7   LTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +T+ N++S + +     LV+FWAPWCGPC+M+ P+IDELA EY GK K  K+NTDE
Sbjct: 80  ITDGNWQSLVIESDTPVLVEFWAPWCGPCRMMHPIIDELAKEYVGKFKCYKLNTDESPST 139

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           + ++GIRSIPT++F KDGE    ++G   K +L   + K L
Sbjct: 140 ATRYGIRSIPTVIFFKDGEKKDAIIGSVPKASLITTIEKFL 180
```

sp Q9S386 THIO_LISMO **Thioredoxin (Trx) [trxA] [Listeria monocytogenes, Listeria innocua]** 103 AA align

```
 Score =  103 bits (258), Expect = 4e-22
 Identities = 46/98 (46%), Positives = 63/98 (63%)

Query: 6   ELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
           E+T+  FE    +G+ L DFWA WCGPC+M++PV++E+  E     KI K++ DE  E
Sbjct: 4   EITDATFEQETSEGLVLTDFWATWCGPCRMVAPVLEEIQEERGEALKIVKMDVDENPETP 63

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
             FG+ SIPTLL  KDGEVV  ++G + K  L E +NK
Sbjct: 64  GSFGVMSIPTLLIKKDGEVVETIIGYRPKEELDEVINK 101
```

tr Q720J6 **Thioredoxin [trx-1] [Listeria monocytogenes (serotype 4b / strain F2365)]** 103 AA align

```
 Score =  103 bits (258), Expect = 4e-22
 Identities = 46/98 (46%), Positives = 63/98 (63%)

Query: 6   ELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
           E+T+  FE    +G+ L DFWA WCGPC+M++PV++E+  E     KI K++ DE  E
Sbjct: 4   EITDATFEQETSEGLVLTDFWATWCGPCRMVAPVLEEIQEERGEALKIVKMDVDENPETP 63

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
             FG+ SIPTLL  KDGEVV  ++G + K  L E +NK
Sbjct: 64  GSFGVMSIPTLLIKKDGEVVETIIGYRPKEELDEVINK 101
```

tr Q8YE56 **THIOREDOXIN C-1 [BMEI2022] [Brucella melitensis]** 107 AA align

```
 Score =  103 bits (257), Expect = 6e-22
 Identities = 47/97 (48%), Positives = 66/97 (67%), Gaps = 2/97 (2%)

Query: 5   IELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +++   NF+S + +     +VDFWA WCGPCK ++P +DE+A+E  G+ KI K VN DE
Sbjct: 4   VKVDNSNFQSDVLQSSEPVVVDFWAEWCGPCKTIAPALDEIAAEMAGQVKIAKVNIDENP 63
```

```
Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKE 99
           EL+A+FG+RSIPTLL  KDGE+   +VG   K  L +
Sbjct: 64  ELAAQFGVRSIPTLLMFKDGELAANMVGAAPKSRLAD 100
```

tr Q8FXY9 **Thioredoxin [trx-1] [Brucella suis]** 107 AA align

```
 Score =  103 bits (257), Expect = 6e-22
 Identities = 47/97 (48%), Positives = 66/97 (67%), Gaps = 2/97 (2%)

Query: 5   IELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +++   NF+S + +     +VDFWA WCGPCK ++P +DE+A+E  G+ KI KVN DE
Sbjct: 4   VKVDNSNFQSDVLQSSEPVVVDFWAEWCGPCKTIAPALDEIAAEMAGQVKIAKVNIDENP 63

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKE 99
           EL+A+FG+RSIPTLL  KDGE+   +VG   K  L +
Sbjct: 64  ELAAQFGVRSIPTLLMFKDGELAANMVGAAPKSRLAD 100
```

tr Q835H2 **Thioredoxin [trx] [Enterococcus faecalis (Streptococcus faecalis)]** 104 AA align

```
 Score =  103 bits (257), Expect = 6e-22
 Identities = 48/100 (48%), Positives = 69/100 (69%), Gaps = 1/100 (1%)

Query: 7   LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEELS 65
           +T+++F +   +G+ L+DFWA WCGPC+M +P++++L+ EY E + KI K++ DE
Sbjct: 5   ITDKDFATETDEGLVLIDFWATWCGPCRMQAPILEQLSEEYDEDEVKIVKMDVDENPATP 64

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           A FGI SIPTLL  KDGEVV + VGV TK  L+  + K L
Sbjct: 65  ASFGIMSIPTLLLKKDGEVVEKAVGVHTKDQLQAMIAKHL 104
```

sp P33791 THIO_STRAU **Thioredoxin (TRX) (Fragment) [trxA] [Streptomyces aureofaciens]** 106 AA align

```
 Score =  103 bits (256), Expect = 7e-22
 Identities = 49/103 (47%), Positives = 69/103 (66%), Gaps = 2/103 (1%)

Query: 5   IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +++T   F+S + +     LV F  PWCGPCKM++PV+DE+A+EYEGK K+ KVNTDE
Sbjct: 4   VKVTNATFKSDVLESDKPVLVHFEGPWCGPCKMVAPVLDEIANEYEGKVKVAKVNTDENP 63

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           +L++++G+RSIPT L  K GEV   +VG   K  L   L  L
Sbjct: 64  QLASQYGVRSIPTRLMFKGGEVAANMVGAAPKTRLAAFLDASL 106
```

sp P07591 THIM_SPIOL **Thioredoxin M-type, chloroplast precursor (TRX-M) [Spinacia oleracea (Spinach)]** 181 AA align

Score = 102 bits (255), Expect = 1e-21
Identities = 44/84 (52%), Positives = 60/84 (71%)

```
Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           +VDFWAPWCGPCK+++PVIDELA EY GK  + K+NTDE   ++ ++ IRSIPT+LF K+
Sbjct: 96  MVDFWAPWCGPCKLIAPVIDELAKEYSGKIAVYKLNTDEAPGIATQYNIRSIPTVLFFKN 155

Query: 82  GEVVHQLVGVQTKVALKEQLNKLL 105
           GE    ++G   K  L + + K L
Sbjct: 156 GERKESIIGAVPKSTLTDSIEKYL 179
```

sp Q41864 THIM_MAIZE **Thioredoxin M-type, chloroplast precursor (TRX-M) [TRM1] [Zea mays (Maize)]** 167 AA align

Score = 102 bits (255), Expect = 1e-21
Identities = 44/85 (51%), Positives = 60/85 (69%)

```
Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           LV+FWAPWCGPC+M++PVIDELA +Y GK   CKVNTD+   +++ +GIRSIPT+L  K
Sbjct: 81  LVEFWAPWCGPCRMIAPVIDELAKDYAGKITCCKVNTDDSPNVASTYGIRSIPTVLIFKG 140

Query: 82  GEVVHQLVGVQTKVALKEQLNKLLG 106
           GE    ++G   K  L   ++K +G
Sbjct: 141 GEKKESVIGAVPKSTLTTLIDKYIG 165
```

tr Q81L73 **Thioredoxin [trx] [Bacillus anthracis]** 104 AA align

Score = 102 bits (254), Expect = 1e-21
Identities = 44/99 (44%), Positives = 68/99 (68%)

```
Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +   +++F +   +GV L+DFWAPWCGPCKM++PV++E+ +E   K K+ KV+ DE +E
Sbjct: 4   VNANDQSFAAETSEGVVLLDFWAPWCGPCKMIAPVLEEIDAELGEKVKVVKVDVDENQET 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           + +F + SIP L   KDG+VV Q +G + K AL E ++K
Sbjct: 64  ARQFEVMSIPALFVLKDGKVVDQALGYKPKEALVELVSK 102
```

tr Q817L8 **Thioredoxin [BC4521] [Bacillus cereus (strain ATCC 14579 / DSM 31)]** 104 AA align

Score = 102 bits (254), Expect = 1e-21

```
 Identities = 44/99 (44%), Positives = 68/99 (68%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +   +++F +   +GV L+DFWAPWCGPCKM++PV++E+ +E   K K+ KV+ DE +E
Sbjct: 4   VNANDQSFAAETSEGVVLLDFWAPWCGPCKMIAPVLEEIDAELGEKVKVVKVDVDENQET 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           + +F + SIP L   KDG+VV Q +G + K AL E ++K
Sbjct: 64  ARQFEVMSIPALFVLKDGKVVDQALGYKPKEALVELVSK 102
```

tr Q72ZM0 **Thioredoxin [trx] [Bacillus cereus (strain ATCC 10987)]** 104 AA align

```
 Score =  102 bits (254), Expect = 1e-21
 Identities = 44/99 (44%), Positives = 68/99 (68%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +   +++F +   +GV L+DFWAPWCGPCKM++PV++E+ +E   K K+ KV+ DE +E
Sbjct: 4   VNANDQSFAAETSEGVVLLDFWAPWCGPCKMIAPVLEEIDAELGEKVKVVKVDVDENQET 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           + +F + SIP L   KDG+VV Q +G + K AL E ++K
Sbjct: 64  ARQFEVMSIPALFVLKDGKVVDQALGYKPKEALVELVSK 102
```

tr Q6HD04 **Thioredoxin [trxA] [Bacillus thuringiensis serovar konkukian str. 97-27]** 104 AA align

```
 Score =  102 bits (254), Expect = 1e-21
 Identities = 44/99 (44%), Positives = 68/99 (68%)

Query: 5   IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +   +++F +   +GV L+DFWAPWCGPCKM++PV++E+ +E   K K+ KV+ DE +E
Sbjct: 4   VNANDQSFAAETSEGVVLLDFWAPWCGPCKMIAPVLEEIDAELGEKVKVVKVDVDENQET 63

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           + +F + SIP L   KDG+VV Q +G + K AL E ++K
Sbjct: 64  ARQFEVMSIPALFVLKDGKVVDQALGYKPKEALVELVSK 102
```

tr Q8EJQ6 **Thioredoxin 1 [trxA] [Shewanella oneidensis]** 108 AA align

```
 Score =  102 bits (253), Expect = 2e-21
 Identities = 46/97 (47%), Positives = 66/97 (67%), Gaps = 2/97 (2%)

Query: 5   IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           I L++++FE+ + K     LVDFWA WCGPCKM++P++D++A EY G+  I K+N D+
Sbjct: 6   IYLSDDSFENDVLKADLPVLVDFWAEWCGPCKMIAPILDDVAEEYAGRVTIAKLNVDQNN 65

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKE 99
           ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKE
```

```
             AK+G+R IPTLL  K+GE+    VG  +K  LKE
Sbjct: 66  VSPAKYGVRGIPTLLLFKNGELAATKVGALSKTQLKE 102
```

tr Q8DSD2 **Putative thioredoxin [trxA] [Streptococcus mutans]** 104 AA
align

```
 Score =  102 bits (253), Expect = 2e-21
 Identities = 48/93 (51%), Positives = 64/93 (68%), Gaps = 1/93 (1%)

Query: 7  LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEELS 65
          +T+  FE+   KG+ LVDFWA WCGPC M +P++++L+ E  E + KI K++ DE    +
Sbjct: 5  VTDATFEAETAKGLVLVDFWATWCGPCLMQAPILEQLSEELDEDELKIVKLDVDENPNTA 64

Query: 66 AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALK 98
            FGI SIPTLLF KDGEVV Q+ GV TK  +K
Sbjct: 65 QNFGIMSIPTLLFKKDGEVVKQVAGVHTKDQIK 97
```

tr Q8L1N0 **Thioredoxin [trxA] [Buchnera aphidicola (subsp. Pemphigus spyrothecae)]** 110 AA
align

```
 Score =  102 bits (253), Expect = 2e-21
 Identities = 46/103 (44%), Positives = 68/103 (65%), Gaps = 2/103 (1%)

Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
          I + EENFE  I  +K   LVDFWA WC PCK+L+P+++E+A+EY+ K  + K+N DE
Sbjct: 7   INVNEENFEKNILQEKNFILVDFWAEWCNPCKILAPILEEIANEYQDKLIVAKINIDENP 66

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
            ++ K+ IR IP LL  K+G ++   +G  +K+ L+  LNK L
Sbjct: 67  NIAPKYSIRGIPALLLFKNGTLLKTKIGALSKIQLQTFLNKYL 109
```

tr Q8P4D3 **Thioredoxin [trxA] [Xanthomonas campestris (pv. campestris)]** 113 AA
align

```
 Score =  101 bits (252), Expect = 2e-21
 Identities = 45/85 (52%), Positives = 59/85 (68%)

Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
          LVDFWA WCGPCKM++PV+D+LA  Y+GK K+ KVN D+   L+ K+ +RSIP LL  KD
Sbjct: 25  LVDFWAEWCGPCKMIAPVLDDLADTYQGKLKVAKVNVDQNRALAIKYHVRSIPMLLLFKD 84

Query: 82  GEVVHQLVGVQTKVALKEQLNKLLG 106
          GEV    +G   K  L + ++K LG
Sbjct: 85  GEVQASQIGAVGKGQLTQMIDKTLG 109
```

tr Q7M0Y9 **Thioredoxin [Clostridium pasteurianum]** 104 AA
align

Score = 101 bits (252), Expect = 2e-21
Identities = 50/99 (50%), Positives = 65/99 (65%), Gaps = 1/99 (1%)

```
Query: 6   ELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
           ++ + NF+  +K G  +VDFWA WCGPCKML PVIDE  SE +GK  I KVN D    ++
Sbjct: 4   DINDSNFQEEVKAGTVVVDFWAAWCGPCKMLGPVIDEDLSEEQGKLDIAKVNVDTNPIVA 63

Query: 66  AKFGIRSIPTLLFTKDGEVVHQ-LVGVQTKVALKEQLNK 103
           ++F I SIPT+L  K+G+V  + LVG   K  LKE L K
Sbjct: 64  SRFEIASIPTVLVFKNGQVADETLVGFAPKGRLKEVLQK 102
```

tr Q88CG6 **Thioredoxin [trx-2] [Pseudomonas putida (strain KT2440)]** 109 AA
align

Score = 101 bits (251), Expect = 3e-21
Identities = 46/93 (49%), Positives = 64/93 (68%), Gaps = 2/93 (2%)

```
Query: 7   LTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
           +T+ +FE+ + K  G  LVD+WA WCGPCKM++PV+D++AS YEGK  + K+N DE +E
Sbjct: 9   VTDASFEADVLKAEGAVLVDYWAEWCGPCKMIAPVLDDIASTYEGKLTVAKLNIDENQET 68

Query: 65  SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
            AK G+R IPTL+  K+G V    VG  +K  L
Sbjct: 69  PAKHGVRGIPTLMLFKNGNVEATKVGALSKSQL 101
```

tr Q83A24 **Thioredoxin [trx] [Coxiella burnetii]** 112 AA
align

Score = 100 bits (250), Expect = 4e-21
Identities = 47/105 (44%), Positives = 68/105 (64%), Gaps = 2/105 (1%)

```
Query: 3   HYIELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDE 60
           H    ++ENFE+ + +     LVDFWA WC PCKM+SPV++E+A EY G+ K+ K+N DE
Sbjct: 4   HVHTASDENFETEVLQADMPVLVDFWAEWCQPCKMISPVVEEIAKEYAGRVKVFKLNVDE 63

Query: 61  QEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
             +   K+G+R IP+LL  ++GEVV + VG   K  L   L++ L
Sbjct: 64  NAQTPTKYGVRGIPSLLIFREGEVVDRKVGALNKSQLAAFLDESL 108
```

tr Q72HU9 **Thioredoxin [TTC1385] [Thermus thermophilus (strain HB27 / ATCC BAA-163 / DSM 7039)]** 110 AA
align

Score = 100 bits (250), Expect = 4e-21
Identities = 44/106 (41%), Positives = 73/106 (68%), Gaps = 1/106 (0%)

```
Query: 1   MSHYIELTEENFESTI-KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTD 59
           M+  IE+T++NF+ T+ +  + LVDFWA WC PC+M++P+++E+A EYEGK  + K++ D
Sbjct: 1   MAKPIEVTDQNFDETLGQHPLVLVDFWAEWCAPCRMIAPILEEIAKEYEGKLLVAKLDVD 60

Query: 60  EQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           E  + + ++ + SIPT++  KDG+ V  LVG Q K   + ++ K L
Sbjct: 61  ENPKTAMRYRVMSIPTVILFKDGQPVEVLVGAQPKRNYQAKIEKHL 106
```

tr Q8UJA6 **Thioredoxin C-1 [trxA] [Agrobacterium tumefaciens (strain C58 / ATCC 33970)]** 106 AA align

```
 Score =  100 bits (248), Expect = 6e-21
 Identities = 46/95 (48%), Positives = 64/95 (66%), Gaps = 2/95 (2%)

Query: 5   IELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +++   NF+S + +     +VDFWA WCGPCKM++P ++E++SE  GK K+ K+N DE
Sbjct: 4   VKVDAANFQSEVLESAEPVVVDFWAEWCGPCKMIAPSLEEISSELAGKVKVAKLNIDENP 63

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
           EL+A+FG+RSIPTL   K GEV    VG   K AL
Sbjct: 64  ELAAQFGVRSIPTLAIFKGGEVADIKVGAAPKTAL 98
```

tr Q97P68 **Thioredoxin [SP1776] [Streptococcus pneumoniae]** 104 AA align

```
 Score =  100 bits (248), Expect = 6e-21
 Identities = 48/99 (48%), Positives = 64/99 (64%), Gaps = 1/99 (1%)

Query: 7   LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEELS 65
           +T+  FE   K G+ LVDFWA WCGPC+M  P++D+L+ E  E   KI K++ DE    +
Sbjct: 5   ITDATFEQETKDGLVLVDFWATWCGPCRMQGPILDKLSEELSEDVLKIVKMDVDENPNTA 64

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
             FGI SIPTLLF KDG+VV Q+ GV T   +K  + +L
Sbjct: 65  RAFGIMSIPTLLFKKDGQVVKQVAGVHTAEQIKAIIAEL 103
```

tr Q7D2B9 **AGR_C_37p [AGR_C_37] [Agrobacterium tumefaciens (strain C58 / ATCC 33970)]** 133 AA align

```
 Score =  100 bits (248), Expect = 6e-21
 Identities = 46/95 (48%), Positives = 64/95 (66%), Gaps = 2/95 (2%)

Query: 5   IELTEENFESTIKKGV--ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +++   NF+S + +     +VDFWA WCGPCKM++P ++E++SE  GK K+ K+N DE
Sbjct: 31  VKVDAANFQSEVLESAEPVVVDFWAEWCGPCKMIAPSLEEISSELAGKVKVAKLNIDENP 90

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
           EL+A+FG+RSIPTL   K GEV    VG   K AL
```

```
Sbjct: 91  ELAAQFGVRSIPTLAIFKGGEVADIKVGAAPKTAL 125
```

sp Q92JR5 **Thioredoxin (TRX) [trxA] [Rickettsia conorii]** 105 AA
THIO_RICCN align

```
 Score = 99.8 bits (247), Expect = 8e-21
 Identities = 46/97 (47%), Positives = 66/97 (67%), Gaps = 6/97 (6%)

Query: 13  ESTIKKGV------ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           +S+ KK V       LVDFWA WCGPCKML+P+IDE++ E +GK K+ K+N DE     +
Sbjct: 7   DSSFKKEVLESDLPVLVDFWAEWCGPCKMLTPIIDEISKELQGKVKVLKMNIDENPNTPS 66

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           ++GIRSIPT++  K+GE      +G+Q K +L + +NK
Sbjct: 67  EYGIRSIPTIMLFKNGEQKDTKIGLQQKNSLLDWINK 103
```

tr Q8DNP9 **Thioredoxin reductase (EC 1.6.4.5) [trxA] [Streptococcus pneumoniae (strain ATCC BAA-255 / R6)]** 104 AA align

```
 Score = 99.8 bits (247), Expect = 8e-21
 Identities = 48/99 (48%), Positives = 64/99 (64%), Gaps = 1/99 (1%)

Query: 7   LTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEY-EGKAKICKVNTDEQEELS 65
           +T+  FE   K G+ LVDFWA WCGPC+M  P++D+L+ E  E   KI K++ DE     +
Sbjct: 5   ITDATFEQETKDGLVLVDFWATWCGPCRMQGPILDKLSEELSEDVLKIVKMDVDENPNTA 64

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKL 104
             FGI SIPTLLF KDG+VV Q+ GV T   +K  + +L
Sbjct: 65  RAFGIMSIPTLLFKKDGQVVKQVAGVHTVEQIKAIIAEL 103
```

tr Q7PAB0 **Thioredoxin [rsib_orf.717] [Rickettsia sibirica]** 105 AA
align

```
 Score = 99.8 bits (247), Expect = 8e-21
 Identities = 46/97 (47%), Positives = 66/97 (67%), Gaps = 6/97 (6%)

Query: 13  ESTIKKGV------ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSA 66
           +S+ KK V       LVDFWA WCGPCKML+P+IDE++ E +GK K+ K+N DE     +
Sbjct: 7   DSSFKKEVLESDLPVLVDFWAEWCGPCKMLTPIIDEISKELQGKVKVLKMNIDENPNTPS 66

Query: 67  KFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
           ++GIRSIPT++  K+GE      +G+Q K +L + +NK
Sbjct: 67  EYGIRSIPTIMLFKNGEQKDTKIGLQQKNSLLDWINK 103
```

tr Q9JYY9 **Thioredoxin [NMB1366] [Neisseria meningitidis (serogroup B)]** 110 AA

align

```
 Score = 99.4 bits (246), Expect = 1e-20
 Identities = 39/73 (53%), Positives = 57/73 (77%)

Query: 22 LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
          L+DFWAPWCGPCKM++P++D++A+E+EG+ K+ K+N D+ E   ++FG+R IPTL+  K+
Sbjct: 26 LLDFWAPWCGPCKMIAPILDDIAAEFEGRLKVVKINIDDNEATPSRFGVRGIPTLMVFKN 85

Query: 82 GEVVHQLVGVQTK 94
          GEVV   VG   K
Sbjct: 86 GEVVATKVGALAK 98
```

tr Q87UQ3 **Thioredoxin [trx-2] [Pseudomonas syringae (pv. tomato)]** 109 AA align

```
 Score = 99.4 bits (246), Expect = 1e-20
 Identities = 46/93 (49%), Positives = 63/93 (67%), Gaps = 2/93 (2%)

Query: 7  LTEENFESTIKK--GVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
          +T+ +FE+ + K  G  LVD+WA WCGPCKM++PV+DE+A+ Y GK  I K+N DE +E
Sbjct: 9  VTDASFEADVLKADGAVLVDYWAEWCGPCKMIAPVLDEIATTYAGKLTIAKLNIDENQET 68

Query: 65 SAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVAL 97
           AK G+R IPTL+  K+G V    VG  +K  L
Sbjct: 69 PAKHGVRGIPTLMLFKNGNVEATKVGALSKSQL 101
```

sp P80579 THIO_ALIAC **Thioredoxin (TRX) [trxA] [Alicyclobacillus acidocaldarius (Bacillus acidocaldarius)]** 105 AA align

```
 Score = 99.0 bits (245), Expect = 1e-20
 Identities = 47/100 (47%), Positives = 65/100 (65%), Gaps = 1/100 (1%)

Query: 7  LTEENFESTIKKGV-ALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
          LT+ NF+  I+     LVDFWA WCGPC+M++PV++E A  +  K  + K+N DE  E +
Sbjct: 5  LTDANFQQAIQGDKPVLVDFWAAWCGPCRMMAPVLEEFAEAHADKVTVAKLNVDENPETT 64

Query: 66 AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
          ++FGI SIPTL+  K G  V QL+G Q K  L+ QL  +L
Sbjct: 65 SQFGIMSIPTLILFKGGRPVKQLIGYQPKEQLEAQLADVL 104
```

tr Q8RAI5 **Thiol-disulfide isomerase and thioredoxins [TrxA2] [Thermoanaerobacter tengcongensis]** 223 AA align

```
 Score = 99.0 bits (245), Expect = 1e-20
 Identities = 45/103 (43%), Positives = 70/103 (67%), Gaps = 2/103 (1%)

Query: 5  IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
          + +T +N+E  +       L+DFWA WC PC++++P+I+ELA EYEGK K+ KVN DE++
```

```
Sbjct: 4   VVITSKNWEEEVVNSDVPVLIDFWAEWCMPCRLVAPIIEELAKEYEGKIKVGKVNVDEED 63

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           EL+ KF I SIPT+   K+G++V +L+G + K     + + K L
Sbjct: 64  ELAMKFRIMSIPTIGLFKNGKMVGKLIGARPKADFVKFIEKYL 106


 Score = 96.7 bits (239), Expect = 7e-20
 Identities = 42/103 (40%), Positives = 69/103 (66%), Gaps = 2/103 (1%)

Query: 5   IELTEENFESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           +E+T +N+E  +        L+DFWA WC PC++++P+++ELA EY+G+ K+ KVN DE++
Sbjct: 119 VEITYDNWEEEVVNSDVPVLIDFWAEWCAPCRLVAPIVEELAHEYKGRLKVGKVNVDEEQ 178

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           EL+ KF I SIPT+   K G++V +++G + K     + + K L
Sbjct: 179 ELAMKFRIMSIPTIGLFKKGKMVDKIIGARPKADFVRFIEKHL 221
```

tr Q8PFZ2 **Thioredoxin [trxA] [Xanthomonas axonopodis (pv. citri)]** 113 AA align

```
 Score = 99.0 bits (245), Expect = 1e-20
 Identities = 43/85 (50%), Positives = 59/85 (68%)

Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           LVDFWA WCGPCKM++PV+D+LA  Y+G+ K+ KVN D+   L+ K+ +RSIP LL  KD
Sbjct: 25  LVDFWAEWCGPCKMIAPVLDDLADTYQGRLKVAKVNVDQNRALAIKYHVRSIPMLLLFKD 84

Query: 82  GEVVHQLVGVQTKVALKEQLNKLLG 106
           G+V    +G   K  L + ++K LG
Sbjct: 85  GQVQATQIGAVGKGQLTQMIDKTLG 109
```

tr Q8F4W0 **Thioredoxin (TRX) [trxA] [Leptospira interrogans]** 119 AA align

```
 Score = 99.0 bits (245), Expect = 1e-20
 Identities = 41/98 (41%), Positives = 66/98 (66%)

Query: 6   ELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
           E+ + NF+S    G+ L+D WA WCGPC+M++PV++EL+ E +G  KI K+N D+ ++ +
Sbjct: 20  EVNDTNFKSETSGGLVLIDCWAEWCGPCRMVAPVLEELSGELDGLVKIKKLNVDDNQDTA 79

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
              GI SIPTLL  KDG++V +++G   K  +K + + +
Sbjct: 80  QSLGISSIPTLLLYKDGQLVDKVIGALPKAQIKNFIER 117
```

tr Q72QY0 **Thioredoxin [trxA] [Leptospira interrogans (serogroup Icterohaemorrhagiae / serovar Copenhageni)]** 104 AA align

```
 Score = 99.0 bits (245), Expect = 1e-20
```

```
 Identities = 41/98 (41%), Positives = 66/98 (66%)

Query: 6   ELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELS 65
           E+ + NF+S    G+ L+D WA WCGPC+M++PV++EL+ E +G  KI K+N D+ ++ +
Sbjct: 5   EVNDTNFKSETSGGLVLIDCWAEWCGPCRMVAPVLEELSGELDGLVKIKKLNVDDNQDTA 64

Query: 66  AKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNK 103
              GI SIPTLL  KDG++V +++G   K  +K  + +
Sbjct: 65  QSLGISSIPTLLLYKDGQLVDKVIGALPKAQIKNFIER 102
```

tr Q6ME96 **Probable thioredoxin [trxA] [Parachlamydia sp. (strain UWE25) (subsp. Acanthamoeba sp.)]** 106 AA

align

```
 Score = 99.0 bits (245), Expect = 1e-20
 Identities = 39/88 (44%), Positives = 67/88 (75%)

Query: 5  IELTEENFESTIKKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEEL 64
          + L ++NF+ TI +GV LVDF+A WCGPC+M++P++++L++  +GKAK+ K++ D+ +
Sbjct: 6  VHLNDDNFQQTISQGVTLVDFYATWCGPCRMIAPIVEQLSTTLQGKAKVAKLDIDQAQST 65

Query: 65 SAKFGIRSIPTLLFTKDGEVVHQLVGVQ 92
          +A   I S+PTL+  KDG+ V ++VGV+
Sbjct: 66 TADLQITSVPTLIVFKDGKEVKRVVGVK 93
```

sp Q9CM49 THIO_PASMU **Thioredoxin (TRX) [trxA] [Pasteurella multocida]** 106 AA

align

```
 Score = 98.6 bits (244), Expect = 2e-20
 Identities = 41/82 (50%), Positives = 59/82 (71%)

Query: 22  LVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFGIRSIPTLLFTKD 81
           L+DFWAPWCGPC+M+SP++DE+A+E+ GK K+ K+N DE +   A+ G+RSIPTL+  K+
Sbjct: 23  LLDFWAPWCGPCRMISPILDEIAAEFSGKVKVVKINIDENQATPAQLGVRSIPTLVLFKN 82

Query: 82  GEVVHQLVGVQTKVALKEQLNK 103
           G+ V   VG   K  L   +N+
Sbjct: 83  GKAVATQVGALPKNQLANFINQ 104
```

sp Q7M1B9 THIO_CHLAU **Thioredoxin (TRX) [trxA] [Chloroflexus aurantiacus]** 109 AA

align

```
 Score = 98.6 bits (244), Expect = 2e-20
 Identities = 42/103 (40%), Positives = 70/103 (67%), Gaps = 2/103 (1%)

Query: 5   IELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQE 62
           IE+ + +F   +   K   +VDFWAPWCGPC++++P++D+LA EY G+  I K VNTD+
Sbjct: 4   IEVHDSDFAEKVLQSKTPVVVDFWAPWCGPCRVIAPILDKLAGEYAGRLTIAKVNTDDNV 63

Query: 63  ELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
```

```
           + +++ G++ +PTL+  KDG  V +LVG + +   +E  +K+L
Sbjct: 64  QYASQLGLKGLPTLVIFKDGREVGRLVGARPEAMYREIFDKVL 106
```

tr Q8ZMX4 **Thioredoxin 2, redox factor [trxC] [Salmonella typhimurium]** 139 AA

align

```
 Score = 98.6 bits (244), Expect = 2e-20
 Identities = 46/102 (45%), Positives = 64/102 (62%), Gaps = 1/102 (0%)

Query: 5   IELTEENFESTIKKGVALV-DFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEE 63
           I  T E  +  +K  + +V DFWAPWCGPC+  +P+ +++A E  GK +  KVNT+ + E
Sbjct: 38  INATGETLDKLLKDDLPVVIDFWAPWCGPCRNFAPIFEDVAEERSGKVRFVKVNTEAERE 97

Query: 64  LSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           LSA+FGIRSIPT++  K G+VV  L G   K      LN+ L
Sbjct: 98  LSARFGIRSIPTIMIFKHGQVVDMLNGAVPKAPFDSWLNEAL 139
```

tr Q9JTY5 **Thioredoxin I [trxA] [Neisseria meningitidis (serogroup A)]** 110 AA

align

```
 Score = 98.6 bits (244), Expect = 2e-20
 Identities = 41/85 (48%), Positives = 61/85 (71%), Gaps = 2/85 (2%)

Query: 12 FESTIKKG--VALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNTDEQEELSAKFG 69
          FE  + K     L+DFWAPWCGPCKM++P++D++A+E+EG+ K+ K+N D+ E   ++FG
Sbjct: 14 FEQDVLKSDLPVLLDFWAPWCGPCKMIAPILDDIAAEFEGRLKVVKINIDDNEATPSRFG 73

Query: 70 IRSIPTLLFTKDGEVVHQLVGVQTK 94
          +R IPTL+  K+G+VV   VG   K
Sbjct: 74 VRGIPTLMVFKNGDVVATKVGALAK 98
```

tr Q8NL58 **Thiol-disulfide isomerase and thioredoxins [Cg13091] [Corynebacterium glutamicum (Brevibacterium flavum)]** 124 AA align

```
 Score = 98.6 bits (244), Expect = 2e-20
 Identities = 48/107 (44%), Positives = 69/107 (63%), Gaps = 2/107 (1%)

Query: 1   MSHYIELTEENFESTI--KKGVALVDFWAPWCGPCKMLSPVIDELASEYEGKAKICKVNT 58
           MS+ + +TE+ F+ST+       +VDFWA WCGPCK LSP+I+E+A EY  KA +  V+
Sbjct: 18  MSNVVAVTEQTFKSTVIDSDKPVIVDFWAEWCGPCKKLSPIIEEIAGEYGDKAVVASVDV 77

Query: 59  DEQEELSAKFGIRSIPTLLFTKDGEVVHQLVGVQTKVALKEQLNKLL 105
           D +  L A F I SIP++L  K+G  V + VG++ K  + E+L K L
Sbjct: 78  DAERTLGAMFQIMSIPSVLIFKNGAKVEEFVGLRPKNEIVEKLEKHL 124
```

Database: EXPASY/UniProt
Posted date: Aug 29, 2004 10:26 AM

```
  Number of letters in database: 494,584,931
  Number of sequences in database:  1,544,870

Lambda     K      H
   0.316    0.135    0.395

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
length of query: 106
length of database: 494,584,931
effective HSP length: 82
effective length of query: 24
effective length of database: 367,905,591
effective search space: 8829734184
effective search space used: 8829734184
T: 11
A: 40
X1: 16 ( 7.3 bits)
X2: 38 (14.6 bits)
X3: 64 (24.7 bits)
S1: 41 (21.6 bits)
S2: 66 (30.0 bits)
```

ExPASy Home page	Site Map	Search ExPASy	Contact us	Proteomics tools	Swiss-Prot

Search in Swiss-Prot and TrEMBL for: thioredoxin helicobacter

Swiss-Prot Release 44.4 of 31-Aug-2004
TrEMBL Release 27.4 of 31-Aug-2004

- Number of sequences found in Swiss-Prot$_{(3)}$ and TrEMBL$_{(7)}$: **10**
- Note that the selected sequences can be saved to a file to be later retrieved; to do so, go to the bottom of this page.
- For more directed searches, you can use the Sequence Retrieval System SRS.

Search in Swiss-Prot: There are matches to 3 out of 158010 entries

THIO_HELPY (**P56430**)
Thioredoxin (TRX). {GENE: Name=trxA; OrderedLocusNames=HP0824, JHP0763} - Helicobacter pylori (Campylobacter pylori), Helicobacter pylori J99 (Campylobacter pylori J99)

TRXB_HELPJ (**Q9ZL18**)
Thioredoxin reductase (EC 1.8.1.9) (TRXR). {GENE: Name=trxB; OrderedLocusNames=JHP0764} - Helicobacter pylori J99 (Campylobacter pylori J99)

TRXB_HELPY (**P56431**)
Thioredoxin reductase (EC 1.8.1.9) (TRXR). {GENE: Name=trxB; OrderedLocusNames=HP0825} - Helicobacter pylori (Campylobacter pylori)

Search in TrEMBL: There are matches to 7 out of 1377572 entries

O25779
Thioredoxin reductase (TrxB) {GENE:OrderedLocusNames=HP1164} - Helicobacter pylori (Campylobacter pylori)

O25996
Thioredoxin {GENE:OrderedLocusNames=HP1458} - Helicobacter pylori (Campylobacter pylori)

Q7VH07
Thioredoxin {GENE:Name=trxA_1; OrderedLocusNames=HH1160} - Helicobacter hepaticus

Q7VIW8
Thioredoxin reductase TrxB (EC 1.6.4.5) {GENE:Name=trxB_1; OrderedLocusNames=HH0486}

- Helicobacter hepaticus

Q7VK37

Thioredoxin {GENE:Name=trxA_2; OrderedLocusNames=HH0055} - Helicobacter hepaticus

Q9ZJG1

Putative THIOREDOXIN {GENE:OrderedLocusNames=JHP1351} - Helicobacter pylori J99 (Campylobacter pylori J99)

Q9ZK51

Putative THIOREDOXIN REDUCTASE {GENE:Name=trxB_2; OrderedLocusNames=JHP1091} - Helicobacter pylori J99 (Campylobacter pylori J99)

New Search

in Swiss-Prot/TrEMBL by AC, ID, description, gene name, organism

Please do NOT use any boolean operators (and, or, etc.)

If you would like to retrieve all the Swiss-Prot/TrEMBL entries contained in this list , you can enter a file name. These entries will then be saved to a file under this name in the directory `outgoing` of the ExPASy anonymous ftp server, from where you can download it. (Please note that this temporary file will only be kept for 1 week.)

File name:

Format: ◉ Swiss-Prot ○ Fasta

Reset or Create file

InterPro **Thioredoxin-related**

[?] = help

IPR006662 **Thiored**

Matches: 1659 proteins. View matches:

Please be aware that match views for entries matching more than 1000 proteins may be slow.

Overview: sorted by AC, sorted by name, of known structure, grouped by taxonomy

Detailed: sorted by AC, sorted by name, of known structure

Table: For all matching proteins, of known structure

Architectures

Name [?] Thioredoxin-related

Signatures [?]
PF00085;Thioredoxin (1011 proteins)
PR00421;THIOREDOXIN (1487 proteins)
PS00194;THIOREDOXIN (1028 proteins)

Type [?] Domain

Dates [?] 2002-11-12 09:34:22.0 (created)
2002-11-12 09:34:22.0 (modified)

Secondary no. [?] IPR000063

Contains [?] IPR011594; Thioredoxin-like

Found in [?]
IPR001853; DSBA oxidoreductase
IPR004799; Periplasmic protein thiol:disulfide oxidoreductase DsbE
IPR005746; Thioredoxin
IPR010357; Eukaryotic protein of unknown function DUF953

Children [?] [tree] IPR005788; Disulphide isomerase

Parent [?] [tree] IPR006663; Thioredoxin domain 2

Process [?] electron transport (GO:0006118)

Function [?] electron transporter activity (GO:0005489)

Abstract [?]

Thioredoxins [1, 2, 3, 4] are small disulphide-containing redox proteins that have been found in all the kingdoms of living organisms. Thioredoxin serves as a general protein disulphide oxidoreductase. It interacts with a broad range of proteins by a redox mechanism based on reversible oxidation of 2 cysteine thiol groups to a disulphide, accompanied by the transfer of 2 electrons and 2 protons. The net result is the covalent interconversion of a disulphide and a dithiol.

$TR\text{-}S_2 + NADPH + H^+ \rightarrow TR\text{-}(SH)_2 + NADP^+$ (1)

$trx\text{-}S_2 + TR\text{-}(SH)_2 \rightarrow trx\text{-}(SH)_2 + TR\text{-}S_2$ (2)

$Protein\text{-}S_2 + trx\text{-}(SH)_2 \rightarrow Protein\text{-}(SH)_2 + trx\text{-}S_2$ (3)

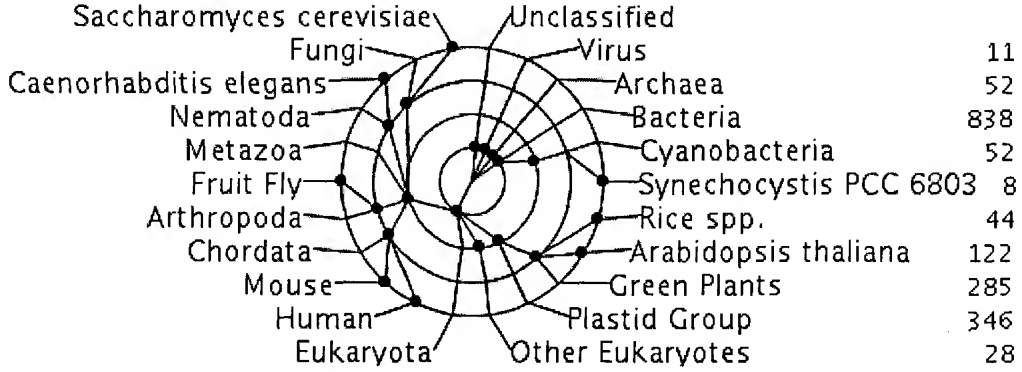
In the NADPH-dependent protein disulphide reduction, thioredoxin reductase (TR) catalyses reduction of oxidised thioredoxin (trx) by NADPH using FAD and its redox-active disulphide (steps 1 and 2). Reduced thioredoxin then directly reduces the disulphide in the substrate protein (step 3) [1]. Protein disulphide isomerase (PDI), a resident foldase of the endoplasmic recticulum, is a multi-functional protein that catalyses the formation and isomerisation of disulphide bonds during protein folding [5, 6]. PDI contains 2 redox active domains, near the N- and C-termini, that are similar to thioredoxin: both contribute to disulphide isomerase activity, but are functionally non-equivalent [6]. Interestingly, a mutant PDI, with all 4 of the active cysteines replaced by serine, displays a low but detectable level of disulphide isomerase activity [6]. Moreover, PDI exhibits chaperone-like activity towards proteins that contain no disulphide bonds, i.e. behaving independently of its disulphide isomerase activity [7]. A number of endoplasmic reticulum proteins that differ from the PDI major isozyme contain 2 (ERp60, ERp5) or 3 (ERp72 [8]) thioredoxin domains; all of them seem to be PDIs. 3D-structures have been determined for a number of thioredoxins [9]. The molecule has a doubly-wound alternating alpha/beta fold, consisting of a 5-stranded parallel beta-sheet core, enclosed by 4 alpha-helices. The active site disulphide is located at the N-terminus of helix 2 in a short segment that is separated from the rest of the helix by a kink caused by a conserved proline. The 4-membered disulphide ring is located on the surface of the protein. A flat hydrophobic surface lies adjacent to the disulphide, which presumably facilitates interaction with other proteins.

One invariant feature of all thioredoxins is a cis-proline located in a loop preceding beta-strand 4. This residue is positioned in van der Waals contact with the active site cysteines and is important both for stability and function [9]. Thioredoxin belongs to a structural family that includes glutaredoxin, glutathione peroxidase, bacterial protein disulphide isomerase DsbA, and the N-terminal domain of glutathione transferase [4]. Thioredoxins have a beta-alpha unit preceding the motif common to all these proteins.

Structural links [?]
PDB 1dby , 1ep7 , 1ep8 , 1f6m , 1f9m , 1faa , 1fb0 , 1fb6 , 1gh2 , 1gl8 , 1keb , 1mek , 1quw , 1srx , 1t7p , 1tho , 1thx , 1tof , 1txx , 1xoa , 2tir , 2trx
CATH 3.40.30.10
SCOP c.47.1.1

Database links [?]
Blocks IPB000063
PROSITE doc PDOC00172

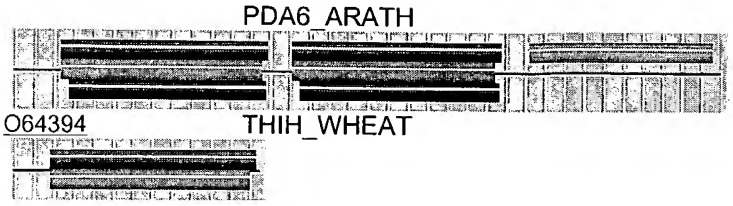
Taxonomy [?]



Examples

O13811 PDI2_SCHPO

O22263



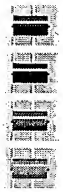
More proteins...

IPR006662 Thioredoxin-related

IPR005788 Disulphide isomerase

IPR006663 Thioredoxin domain 2

IPR011027 Endoplasmic reticulum protein ERP29, C-terminal



Publications

1. Holmgren A.
Thioredoxin.
Annu. Rev. Biochem. 54: 237- 271 (1985) [PubMed: 3896121]
2. Holmgren A.
Thioredoxin and glutaredoxin systems.
J. Biol. Chem. 264: 13963- 13966 (1989) [PubMed: 2668278]
3. Holmgren A.
Thioredoxin structure and mechanism: conformational changes in oxidation of the active-site sulfhydryls to a disulfide.
Structure 3: 239- 243 (1995) [PubMed: 7788289]
4. Martin J.L.
Thioredoxin - a fold for all reasons.
Structure 3: 245- 250 (1995) [PubMed: 7788290]
5. Puig A. , Lyles M.M. , Noiva R. , Gilbert H.F.
The role of the thiol/disulfide centers and peptide binding site in the chaperone and anti-chaperone activities of protein disulfide isomerase.
J. Biol. Chem. 269: 19128- 19135 (1994) [PubMed: 7913469]
6. Lyles M.M. , Gilbert H.F.
Mutations in the thioredoxin sites of protein disulfide isomerase reveal functional nonequivalence of the N- and C-terminal domains.
J. Biol. Chem. 269: 30946- 30952 (1994) [PubMed: 7983029]
7. Song J.L. , Wang C.C.
Chaperone-like activity of protein disulfide-isomerase in the refolding of rhodanese.
Eur. J. Biochem. 231: 312- 316 (1995) [PubMed: 7635143]
8. Mazzarella R.A. , Srinivasan M. , Haugejorden S.M. , Green M.
ERp72, an abundant luminal endoplasmic reticulum protein, contains three copies of the active site sequences of protein disulfide isomerase.
J. Biol. Chem. 265: 1094- 1101 (1990) [PubMed: 2295602]
9. Saarinen M. , Gleason F.K. , Eklund H.
Crystal structure of thioredoxin-2 from Anabaena.
Structure 3: 1097- 1108 (1995) [PubMed: 8590004]

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